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Editorial

THE JOURNAL

The final issue of Volume XV of the Journal brings with it a farewell and a sincere wish for the success of every student at his final examinations in May. Examinations have been described as "a necessary evil" but whatsoever they are, they lend such an atmosphere to our otherwise glorious spring weather, that full appreciation of nature's wonders is made very difficult.

It is hoped that this Journal has served you loyally throughout the year and that its pages have proven instructive and interesting. With the cooperation of the entire staff we succeeded in doubling the size of the Journal over that of other years. In so doing we did not resort to the publishing of irrelevant and unworthy articles but maintained the highest standard possible at all times. The Journal was fortunate in receiving many letters of congratulation throughout the year from graduate subscribers praising the material that was offered and also the successful formation of our new departments. We take this opportunity to thank all those who so kindly wrote in to the Journal—it was just such expressions of commendation that made the Editorial Staff feel that the extra work put into it was worth while.

The Editor wishes to thank the Editorial Staff, our capable Managing Editor and the Circulation Staff for the interest and industry displayed by all. The latter two departments had an optimal turn over in business. It might be of interest to know that we had ninety paid up graduate subscriptions this year with an exchange list that involved many European Universities. The Graduate Advisory Staff cooperated freely in what had to be done and it was by their help that many articles were made available for publication.

The Abstract column, so well handled by Miss McClelland, entailed a great deal of work but it is hoped it served as a useful guide for the student's outside reading. The Staff of men who did this reviewing, A. Goggio, J. D. Duffin, W. G. Rice, M. E. Hall, A. G. MacKinnon, R. A. Mustard, J. G. Reid, E. B. Toveo, F. C. Barton, G. D. Temple, F. L. Lawson and D. H. Copp should be commended for their work.

It is understood that certain students consider the Journal a 'closed corporation' when it comes to obtaining staff positions. Such is not the case however, and besides asking all who are interested in Journalism to apply for positions when these applications are called for, we inform you that changes are at present under consideration for

extension of the staff to make work available to a greater number. In these days of rapidly changing medicine when the scientific periodical has replaced the text book, and everyone seems to be writing, some knowledge of how to properly prepare a scientific paper would appear to be to one's advantage.

Next year the editor's position will be found in the capable hands of John Belton. To assist him Norman Hillary as Managing Editor and Ken Greer as Associate Editor will constitute the remainder of the Editorial Board. Judging from the ability and past record of these men a brilliant season is assured for the Journal next term.

We proffer our thanks to Mr. Avila Paré of the Extension Print whose interest in our Journal has always been appreciated and considered as contributing in a great measure to its annual success.

* * *

GOOD FRIENDS

A word of praise where it is due and a word of advice to all medical students who value friendship and the advantages of counsel and ready assistance which can be derived from same when it is found.

It is not 'news' to many but "the girls in the medical office" Miss Jones, Miss Russell and Miss Perry offer every medical student a ready ear for his troubles and equally ready counsel when such is at all available. Nothing seems to be too much in the way of favors that these grand ladies keep continually bestowing on us medical students. What is friendship more than that, when it is associated with the confidence and genuine interest that is found there? No three persons could display more real interest in the faculty and students. It is thought that perhaps they are more the champion of the student no doubt by virtue of his greater need of a champion and their natural instinct to protect the weak. Their interest in student problems is sincere and with a full knowledge of our various complaints and desires they often aid the process of their solution by a well placed word of explanation.

Impartial in their attitude, provided one is found worthy, they appear, after examinations and before the results come out, somewhat like three great Egyptian sphinxs — knowing all and very sweetly yet firmly saying nothing. When questioned directly for information "on the side" or "before official presentation" the questioner is smiled at very kindly and tolerantly and has things explained to him in a phraseology which through long experience has become most tactful, and in a manner which leaves the matter entirely closed.

It is always a pleasant surprise to be greeted by a smile and called by name on walking into the office in your freshman year—makes one feel one is not entirely a submerged personality in this large college. It must be even more pleasing to be called by name on returning several years after graduation as so often happens when a graduate enters the medical office after a long absence.

Such are Miss Jones, Miss Russell and Miss Perry—they fill a real place in our undergraduate life and will no doubt be remembered long after our graduation. We salute them and wish them all happiness.

* * *

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF CANADA

Attention is drawn to the advertising announcement in this issue of the examinations for fellowship in the Royal College of Physicians and Surgeons of Canada. This announcement is of special interest to Toronto students because this October will find not only the written but oral examinations held in Toronto. As a result of the efforts of the executive and Fellows of the Royal College, this relatively new Society has already established itself

soundly and each year finds an increasing number of candidates at the annual examinations. The stand taken by leading hospitals in Canada, whereby those who have been successful in passing the primary examinations are given special consideration in the matter of hospital appointments, has given added prestige to this degree.

The executive of the R.C.P. & S. of Canada and our own Medical faculty urge all those, who are able, to take the primary examinations at some time after third year and before graduation.

* * *

TUBERCULOSIS AMONG STUDENTS AND INTERNS.

In the February issue of this Journal Editorial comment was made on the problem of Student Health under the title "Hygiene and Preventive Medicine, is it practiced in our University?" What was said there need not be reiterated. Suffice it to say that at the present moment there are few measures in existence in our medical school and in the majority of Toronto Hospitals to attempt the control of this dread disease among medical students and internes.

This situation has been brought to the fore recently by the report of two new cases within a few weeks, one a student and the other an interne at one of the Toronto Hospitals. That brings the grand total of one student, three internes and one nurse afflicted with Tuberculosis within the school term, with still a month and a half to go.

When one realizes that Tuberculosis is preventable and if not preventable then controllable by ensuring early diagnosis of all cases one wonders why further preventive measures should not be instituted. The Association of Canadian Medical Students and Internes, this recently formed group of representatives from all the Eastern Medical Colleges, realizing the need for action, have resolved to meet this situation by calling for assistance from the Provincial Department of Health in hopes of receiving aid from this quarter. The students and internes fully aware of the situation would appreciate any cooperation or action that may be taken by the Faculty or Hospital Boards in Toronto to combat this disease.

PRINCIPLES OF TREATMENT OF CANCER

By W. E. GALLIE, M.D., F.R.C.S.
Professor of Surgery

The key-note of the publications of the many cancer campaigns of the past few years has almost invariably been one of warning, intended to impress on the public the importance of early treatment and the magnitude of the disaster that will certainly attend delay. At the present moment it would seem that all the good that could be expected from such a campaign has been obtained and that the continuance of it is more likely to frighten people than to encourage them to seek treatment. It would seem, therefore, that the time is ripe for uttering a word of encouragement, to indicate that great advances have been made and that all is not lost when cancer has been diagnosed.

True, we do not yet know the cause of cancer but even in this regard great progress is being made which must surely before long reveal to us the secret that will lead to a certain cure. But while admitting that up to the present we do not know what causes the body cells to take on the characteristics of malignancy, and also that we do not know the antidote to those influences, we do know that if all the malignant cells can be removed or destroyed cures can be established which will allow our patients to live in comfort through the normal span of life. It is upon this truth that the modern surgical treatment of cancer and the more recent radiological treatment of it is based and convincing proof of its effectiveness can be seen every day in the follow-up clinics of our hospitals. There one can observe and study steadily increasing numbers of five and ten year cures and among them the formerly hopeless cancers of the breast, the lip and tongue, the colon, the rectum and the uterus.

Surgical Treatment

The surgical treatment of cancer, when aiming at a cure, requires the removal of the primary growth and the lymphatic field which drains it. The realization of this has led to great improvement in surgical technique and has increased enormously the percentage of cures. There is, however, still room for improvement for there is a wide difference in the thoroughness with which these operations are performed. It is not so much in the removal of the primary growth that improvement is required, for this portion of the operation is stereotyped and described in every text-book, but rather in the dissection of the lymphatic field. The difference in the care and skill expended by different operators on the axilla in carcinoma of the breast, on the sides of the neck in carcinoma of the lip or tongue, on the pyloric, coeliac and coronary glandular areas in carcinoma of the stomach, accounts for great differences in final results and indicates that these are operations which should be done only by surgeons of great experience and training. It is utterly wrong and unjustifiable for the occasional operator to accept responsibility for the lives of such patients.

Radiological Treatment

The objective of treatment by radium or X-ray is not the removal of the cancerous growth but the destruction of it and its disseminated cells wherever they may be. This is possible because proliferating cells such as those of cancer are more vulnerable to the rays than normal cells. It has been the constant effort, therefore, of the radiologist to develop rays of sufficient intensity and penetrating power to reach all the cancer cells and to destroy them, without injury to the normal

surrounding tissues. The problem would be simple if there were any uniformity in the radiosensitivity of tumour cells and if there were a wide difference between the sensitivity of cancerous and normal cells. Unfortunately, no such favourable condition exists so that the way of the radiologist has been difficult. He has made enormous steps forward, however, and has accomplished results in certain of the more superficial cancers, such as those of the skin, the lip, the tongue, the larynx and the cervix uteri that leave no doubt of the effectiveness of the treatment. It is rare indeed for such patients to have the primary growth treated surgically.

The great hope of the radiologist is that he will develop his technique with radium or high voltage X-rays to such an extent that he may be able to so increase the penetrating power and effectiveness of his rays that not only the cancer cells in the lymphatic fields may be destroyed but also that distant metastases may be successfully attacked. Research in this direction is at its height at the present time and it is hoped will lead on to success. In the meantime, however, the general consensus of opinion supports the surgical removal of lymphatic fields whether obviously involved or not as this plan yields a certain definite percentage of successes, whereas with radiological treatment the results are so far uncertain. The usual practice, therefore, in cancer of the tongue, floor of the mouth, etc., is to deal with the primary growth with radium and to do block dissections of the glands.

Combined Surgical and Radiological Treatment

While published records of comparative results in groups of cases treated by surgery alone and by surgery combined with postoperative radiation have not been very convincing, there is no doubt that theoretically the exposure of the patient to X-rays soon after the operation should increase the chances of permanent success by destroying cancer cells which may have been left in the wound. The argument in favour of preoperative administration of X-ray is not quite as clear and is, indeed, not strongly supported by the great institutes for radiotherapy, but more information will be available later on. The common practice in hospitals equipped for high voltage X-ray treatment is to proceed with the radical removal of primary growth and lymphatic field, as in carcinoma of the breast, and then to follow on when the wound is healed, with X-ray treatment. The great objection to the plan is that to the strain of a major operation is added a prolonged ordeal of exposures to the rays which is often accompanied by a disagreeable nausea. However, the curative value of the rays is so convincing that few surgeons, nowadays, will risk the omission of postoperative radiation.

Just as in the case of the surgical treatment it is necessary to sound a warning that treatment by irradiation should be solely in the hands of the expert. Radium and the high voltage X-ray tube are powerful instruments which in the hands of the physician or surgeon who has taken special training and thus acquired ripe experience may accomplish great good, but they are also dangerous instruments which in the hands of the inexperienced may do appalling harm. No more misleading statement was ever made than that radium is an instrument which every surgeon should use as he does his scalpel. It could only be true if it were modified to read "that every surgeon who proposes to use radium should take the same sort of training in its use as he did when he was learning to use his scalpel."

Palliative Treatment

Unfortunately many of our patients when they come to us for treatment of cancer have disease which has advanced so far, either by spread of the primary growth or by metastasis to lymphatic glands or more distant organs, that the surgical removal of the whole of the diseased tissue is out of the question,

and the destruction of it by irradiation beyond all possibility. For these unfortunates, however, there is still much that can be done in the way of lengthening life and in making what remains of life more tolerable. The amazing development of surgical technique in the past twenty-five years has made possible the removal of growths such as occur in the stomach, with astounding recoveries. Whereas a few years ago such patients were left to perish miserably in a few months, many of them nowadays survive a gastrectomy and enjoy a year and sometimes several years of good health before the secondaries overwhelm them. It should always be remembered also, that sometimes the removal of a fungating growth from a patient who undoubtedly has metastatic involvement of glands which cannot be removed, seems to give him a new lease of life that can only be explained by the assumption that the cancer cells in the glands are of very low grade or are held in check for long periods of time by some natural mechanism of defense. Similarly, much relief from utter misery can be afforded in cancer of the head of the pancreas by an anastomosis of the gallbladder to the stomach or intestines. And now that the management of a permanent colostomy has been so much improved, this operation has lost many of its objectionable features and is firmly established as a valuable palliative measure, even when the growth cannot be removed.

Similarly, radiotherapy can often be used to lengthen life and relieve pain. While few would expect that deep X-ray therapy could cure a patient with secondaries in the spine, yet there is not a doubt that such treatment will often give great relief from the distressing pain in the back that such tumours produce. It will sometimes so destroy the growth that the X-ray picture will show definite healing of the bone.

What the future holds in the treatment of cancer cannot be foretold. Many think that before long the intensive researches that are being made on the biological nature of cancer will be rewarded by discoveries which will enable us to prevent its development or to cure it when established. This happy moment has not yet arrived, however, so that we must use what measures we have and try to improve them. Fortunately these measures are effective in many cases and offer a strong ray of hope in what was once a hopeless condition.

CRANIO-CEREBRAL INJURIES

PART II.

By KENNETH G. McKENZIE, M.D.

PLAN OF PART II.

A. *Introduction.*
B. *Lesions requiring specific treatment.*
   1. *Lacerated scalp.*
   2. *Compound depressed fractures.*
   3. *Simple depressed fractures.*
   4. *Extra-dural haemorrhage.*
   5. *Sub-dural haemorrhage.*
   6. *Sub-dural Hydroma.*
   7. *Localized intra-cerebral haemorrhage.*
C. *The importance of adequate records.*
D. *Lumbar puncture.*
E. *X-ray examination.*
F. *Cerebro-spinal fluid leak from the ear or naso-pharynx.*
G. *Length of time in bed and advice on discharge.*
H. *The treatment of post-traumatic headache and dizziness.*
I. *Prognosis.*
J. *Medico-legal.*
K. *Differential diagnosis in the unconscious patient with a bruise or cut on the head.*

A. Introduction

In Part 1, of this paper Cranio-cerebral Injuries were classified under two main headings:

GROUP 1. *Patients who remain unconscious for approximately an hour or longer from the time of the accident.*

GROUP 2. *Patients who are dazed or who are recovering consciousness shortly after the accident.*

This classification is a fairly satisfactory clinical one and provides for adequate discussion of the group considered to have a serious cerebral injury, that is, the patient who is immediately rendered unconscious and remains unconscious for a considerable period. (See PART 1).

It has been pointed out in PART 1, of this paper, that it was the exceptional case in *Group* 1, in which specific surgical treatment was indicated. Extra-dural haemorrhage is unusual in *Group* 1. Other space-taking lesions such as sub-dural haemorrhage, sub-dural cerebro-spinal fluid and localized intra-cerebral haemorrhage occur in both groups. When one or more of these four lesions occurs in *Group* 1, it is usually only a part of a much more serious general cerebral injury, so that in actual practice, operation is seldom done on these patients. The indications and time for operation have been covered in *Part* 1, of this paper. On the contrary the diagnosis and treatment of these lesions in *Group* 2, is of the utmost importance as there is usually a period when a successful operation can be performed.

Again simple and compound depressed fractures are more commonly seen in *Group* 2, because when the skull gives way beneath a blow the injury to the brain is most marked beneath the fracture and there is not the widespread injury and contra-coup laceration which cause prolonged loss of consciousness. There are exceptions to this but usually the patient with a depressed fracture shows evidence of recovering consciousness soon after the injury.

About 90% of all cranio-cerebral injuries may be classified under *Group* 2. Fortunately the vast majority of these patients recover and only a very few will require specific surgical treatment because of an intra-cranial space-taking lesion or depressed fracture. After a consideration of these specific surgical conditions the remainder of the paper will deal with problems which are more or less common to all cranio-cerebral injuries.

B. Lesions Requiring Specific Surgical Treatment

1B. Lacerated Scalp.—The treatment of a cut in the scalp requires some

thought and consideration just as a cut over the front of the wrist does. In the latter case important tendons and nerves may be injured, whereas with a scalp wound there may be an underlying fracture. Haemorrhage sufficiently great, to constitute an emergency is controlled by temporary suture or Michei clips and a firm dressing. Careful examination and treatment of the wound is then carried out. Shaving of the scalp about the cut is most satisfactorily carried out with a safety razor blade held in a Kelly clamp and used as a straight razor. Soap is applied with gauze, not a shaving brush which may carry infection from one case to another. The wound is thoroughly cleaned with soap and water, antiseptic solutions such as iodine are avoided because of their injurious effect on tissues. Badly bruised tissues with a poor blood supply are removed. The underlying bone is carefully examined by inspection and palpation for a fracture. If there is a linear fracture, suture of the wound is proceeded with. If there is a depressed fracture a wider shaving of the scalp is carried out while arrangements are made for an operating room to deal with this complication in an adequate manner. If there is not a depressed fracture the edges of the wound are accurately approximated by individual through and through fine silk sutures about a quarter of an inch apart; the accurate approximation of the edges usually controls haemorrhage but occasionally individual vessels must be ligated. It is not necessary or advisable to leave drainage, a procedure which is more likely to promote infection than prevent it. If a haematoma collects beneath the scalp it is better dealt with by aspiration than drainage.

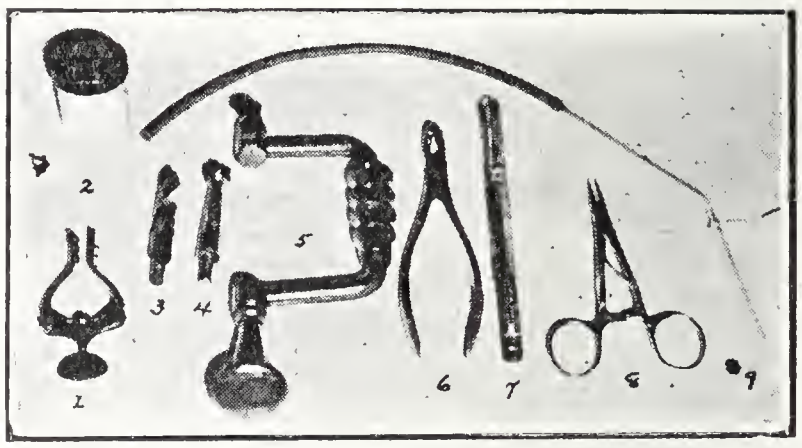

Illustration 6.

1. Mastoid Retractor. 2. Bone Wax. 3, 4 and 5. Hudson Drill and Burrs. 6. Rongeurs. 7. Silver Clips. 8. Silver Clip Forceps. 9. Sucker.

2B. Compound Depressed Fractures.—A depressed fracture is preferably treated in an operating room equipped with a good light—suction apparatus and certain special instruments as shown in Fig. 6. An endothern machine for the control of haemorrhage from dura and brain is also a great asset.

Under local or general anaesthesia steps are taken to deal with the lacerated scalp as previously described. The depressed fragments of bone are thoroughly exposed by turning back the scalp after extending the laceration in various directions being careful to leave the periosteum on the bone about the depressed area. Haemorrhage from the turned back scalp is temporarily controlled by fine artery forceps placed in a row along the galea. The subsequent closure with through and through fine silk sutures will permanently control haemorrhage from the scalp. The depressed fragments of bone are elevated and at least one piece removed to permit examination of the underlying dura. If the dura is intact the fragments of bone may be left. If infection develops the intact dura will protect the cerebro-spinal fluid and brain from infection; although it may be necessary subsequently to remove a dead piece of bone. If the dura has been fragmented and torn the problem is somewhat more difficult. Fragments of bone cut off from their blood supply and which consequently may promote infection are descarded. All debris and foreign material in the brain are carefully washed and sucked away. Oozing from the brain is controlled by the application of cotton pledgets soaked in saline; larger vessels are coagulated, clipped or tied. If the patient has been operated upon within a few hours of the injury and it has been possible to clean up the field thoroughly, the defect in the dura may be closed with a patch of fascia from the thigh or muscle. If heal-

ing without infection is doubtful it is probably safer to leave a soft rubber drain through a stab wound away from the defect in the skull. The overlying scalp is very carefully sutured and firmly supported with a pad held in place by an elastic flannel bandage. Firm healing of the scalp and firm support by the dressing is all important to prevent cerebral herniation. A drainage tube if left, is usually removed at the end of twenty-four hours. At some future date the defect in the bone can be repaired with a celluloid plate. The underlying principles of the whole procedure are to prevent infection by early operation and the removal of all debris and devitalized tissue, and the prevention of cerebral herniation by accurate closure and support of the wound. When these cases are carefully dealt with primary healing usually takes place; if improperly handled death from meningitis may occur or a cerebral fungus or abscess develop.

3B. Simple Depressed Fractures—Operation may be delayed until it is convenient because infection is not a problem, as the fracture is not compound. With a local or general anaesthetic exposure is obtained by turning down a flap of scalp, leaving the periosteum on the bone The depressed area is elevated, detached fragments of bone may be fitted back in place as free grafts. A small opening is made in the dura to rule out an underlying clot. The operation is completed by carrying out a careful scalp closure without drainage, and the application of a firm dressing to prevent the collection of blood beneath the scalp. If a haematoma does develop it is aspirated at the end of twenty-four hours.

One occasionally sees a large depressed fracture in infants following forceps delivery. With local anaesthesia and within a few hours of birth it is a simple matter to spring a large depressed area back into place. A short scalp incision is made at the edge of the depression, and an opening made in the underlying bone with a scalpel—a flat instrument is then slipped between dura and bone to the centre of the depression and elevation is easily accomplished.

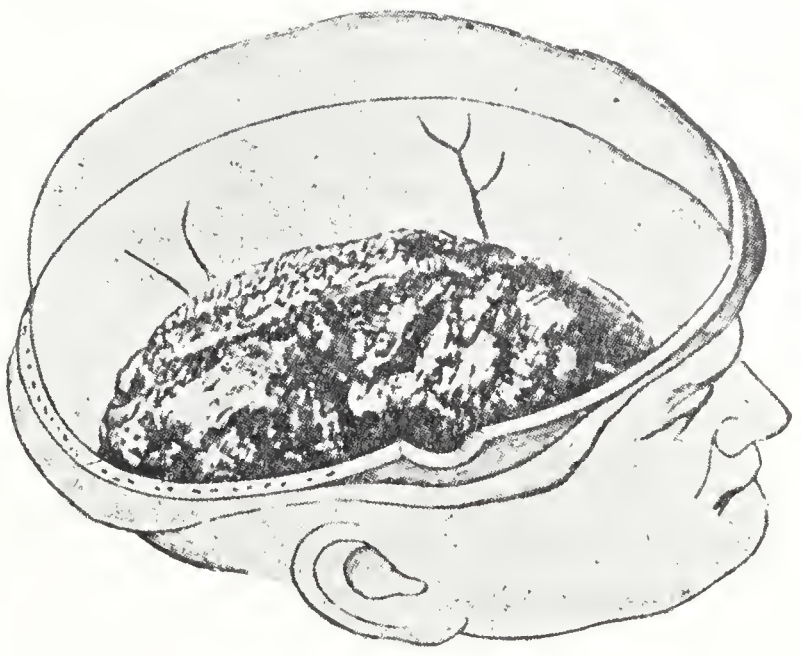

Illustration 7.

Middle meningeal haemorrhage in a patient of Mr. Hilton's. Drawing 80[20] Guy's Hospital Museum.

4B. Extra-dural Haemorrhage.—When a student graduates from medical school in this day and age he will have heard a good deal about extradural haemorrhage, a lesion which usually but not always arises from a rupture of the anterior branch of the middle meningeal artery. Nevertheless the lesion is rare and in a general practice a doctor is not likely to encounter more than one or two cases. If he is to have the satisfaction of saving these few patients he must keep in mind the usual syndrome and also appreciate that there are variations of this syndrome. In a large hospital centre his responsibility is usually one of diagnosis. In outlying districts he must on occasion be prepared to operate, as there may not be time to call a consultant from a distance.

Briefly the syndrome which is impressed on medical students to-day is as follows:

An individual is dazed or rendered unconscious for a few minutes by a blow on the head. Usually recovery occurs without the development of serious symptoms. Such patients, however, should be kept under close obser-

vation and the possibility of extra-dural haemorrhage considered. If a clot is forming in the extra-dural space it usually causes signs of pressure within an hour or two. The most important evidence of this pressure is a dulling of the mental faculties, which steadily progresses to coma with stertorous breathing. Other signs, such as slowing of the pulse and rising of the blood-pressure, are important but frequently there is no record of such changes, because observations had not been possible or accurate during the early period when these signs frequently are present only for a short time. As coma deepens the respiration, pulse and temperature rise, and these changes indicate failure of the medullary centres to respond in the normal physiological way to a rapid increase of intracranial pressure. They are very serious signs and where possible operation should be performed before they develop. During the development of the stupor, examination discloses three lateralizing signs:

a. Oedema of the scalp in the temporal fossa suggesting a linear fracture. This can be confirmed by X-ray examination. If the fracture crosses the groove of the middle meningeal or one of its branches, it is of special significance, as almost always the lesion is produced by a fracture tearing this artery.

b. A dilated fixed pupil on the side of the lesion. This is due to displacement of the brain, which causes stretching and pressure on the third nerve. It is one of the most constant and valuable lateralizing signs.

c. A positive Babinski and diminution of active movement of the arm and leg on the side opposite to the lesion, that is on the side opposite to the dilated fixed pupil. This is due to pressure by the large clot on the underlying cerebral hemisphere. The hemi-paresis often has to be elicited by painful stimuli because the patient is usually stuporous when it develops.

In the presence of the above syndrome, lumbar puncture discloses a high degree of pressure. If the fluid is clear or only slightly bloody the increased pressure is almost certainly due to an extra-dural haemorrhage. On the other hand a very bloody cerebro-spinal fluid indicates some degree of cerebral damage even if there is an extra-dural clot.

Operative and Post-Operative Care.

The whole head is shaved, atropine but no morphia is given. If the patient is in deep coma local infiltration between the scalp and the bone suffices. Usually a general anaesthetic is desirable for two reasons:

a. These patients are apt to become very restless and non-co-operative.

b. A general anaesthetic causes an increased congestion and tension in the brain which is a great aid in bringing the dura up against the bone after the clot has been removed.

In administering the general anaesthetic, whether it be ether, chloroform, or ether and chloroform, it is most important to maintain a free airway. Gas is not a desirable anaesthetic in these cases.

Apart from a good spot light, Fig. 6, shows the special instruments and equipment that are desirable and necessary to perform the operation properly.

Operation.—A short one inch incision is made just above the upper and anterior tip of the ear. The bone is exposed by splitting the temporal muscle; a linear fracture is usually seen at this stage. A self-retaining mastoid retractor is inserted. The bone is perforated by a Hudson burr or circular trepine. If the diagnosis is incorrect the dura is found adjacent to the bone.

If a clot is exposed the operation is proceeded with by enlarging the bone opening to at least an inch and a half in diameter. The clot is removed by suction or finger dissection. Usually a spurting meningeal artery can be located in the exposed dura. To gain access to this artery or to remove all the clot it may be necessary to enlarge the

bone opening still further. The bleeding vessel is controlled by a ligature carefully passed so as not to injure a vessel in the underlying brain. A silver clip, applied and left in position is usually a more efficient and easier method of controlling the vessel. The vessel may be torn very low in the temporal fossa, possibly right at its entrance into the skull through the foramen spinosum; in such a situation the foramen may be plugged with cotton, or the vessel coagulated. Not infrequently one fails to see a definite spurting vessel, this is especially true in the delayed cases. A general ooze from bone and dura is frequently a troublesome feature even in the cases where the main meningeal vessel has been controlled. This is especially so in the delayed cases where the brain is not under tension and does not expand and hold the dura against the bone after the clot is removed. Gentle packing with gauze usually controls oozing. Occasionally it is desirable to make extra burr holes and suture the dura up to the scalp through these openings. Unless the dura comes up snugly against the bone and there is little or no oozing the wound is left fairly well open. At a subsequent dressing in the operating room twenty-four hours later the packing can be all or partly removed and the wound sutured. Occasionally it is necessary to leave the wound partly open for several days, while the packing is gradually being removed.

In the case of a negative exploration a second burr hole should be made farther back over the parietal area. If this is negative the same procedure should be carried out on the other side.

Post-Operative Care.—The patient is put to bed on his side and the head is placed so that the airway is free, if respirations are stertorous this is of the utmost importance. The tongue is kept forward by a suture if necessary. Tubes may be placed in the nose or inside the cheek to increase the airway.

A careful half hour check is kept on the temperature. In the seriously ill patients the heat regulating centres may not function normally, and steps must be taken to control a rising temperature. Sponging may be sufficient; a rectal irrigation with ice water for a temperature above 104° is most efficient and often necessary; a ten or twenty minute irrigation will quickly lower a temperature; it may have to be repeated frequently. The control of hyperthermia is definitely a life saving measure in certain cases.

Re-exploration is indicated if one suspects that the clot has reformed; apart from this there is little else of specific importance except the maintenance of a free airway and the control of hyperthermia; all of these three measures are essential in certain patients.

Summary of Conclusions.

1. Extra-dural haemorrhage is an infrequent lesion.
2. A lucid interval is the most valuable diagnostic sign. It may occasionally be absent.
3. A prolonged lucid interval is not infrequent and may confuse the diagnosis. These cases may become critically ill very rapidly.
4. A dilated pupil is a very valuable diagnostic and lateralizing sign. It may occasionally be absent.
5. Paresis is a valuable diagnostic and lateralizing sign. It may be difficult to establish in a stuporous patient. It may also be a false localizing sign and be on the same side as the lesion, in which case it is usually caused by contre-coup bruising of the hemisphere on the side opposite to the haemorrhage.
6. Clear or faintly blood-tinged cerebrospinal fluid in the presence of a lucid interval followed by stupor makes the diagnosis almost certain; on the other hand if the fluid is very bloody the diagnosis is in doubt as the syndrome may be produced entirely by the bruising or laceration of the brain.
7. A fracture is a valuable diagnostic and lateralizing sign, but it may be almost impossible to see when the

fracture is not next the X-ray plate; careful examination discloses oedema of the scalp overlying a fracture. Cases do occur without a fracture.

8. Extra-dural haemorrhage is a serious lesion. The high mortality rate impresses one with the necessity for accurate early diagnosis and prompt efficient treatment.
9. Bilateral exploratory burr holes should be made if there is a reasonable suspicion of the diagnosis. It is much better to have a negative exploration than an operation carried out too late or not at all.
10. Extra-dural haemorrhage may occur over the cerebellum; or a large extra-dural haemorrhage over the cerebral hemisphere may lift the lateral sinus out of its bed and extend back over the cerebellum.
11. Three pathological lesions may simulate the syndrome of extra-dural haemorrhage:

    a. Bruising and oedema of the brain.
    b. Intra-cerebral haemorrhage.
    c. Acute sub-dural haemorrhage.

In the last analysis exploratory burr holes establish or disprove the diagnosis.

5B. Sub-dural Haemorrhage. — Sub-dural bleeding may occur because of:

1. Tearing of veins as they cross the subdural space from the arachnoid to the longitudinal sinus.

2. Bleeding from veins and arteries that have been ruptured by a superficial tearing and bruising of the arachnoid and brain usually a contre-coup injury.

3. A depressed fracture and tearing of the dura, which permits intradural bleeding from one of the middle meningeal vessels.

4. An artery on the surface of the brain is occasionally held to the dura by an adhesion, a blow may tear an opening in such an artery (observed by the author on one occasion, the bleeding artery was over the centre of the parietal lobe).

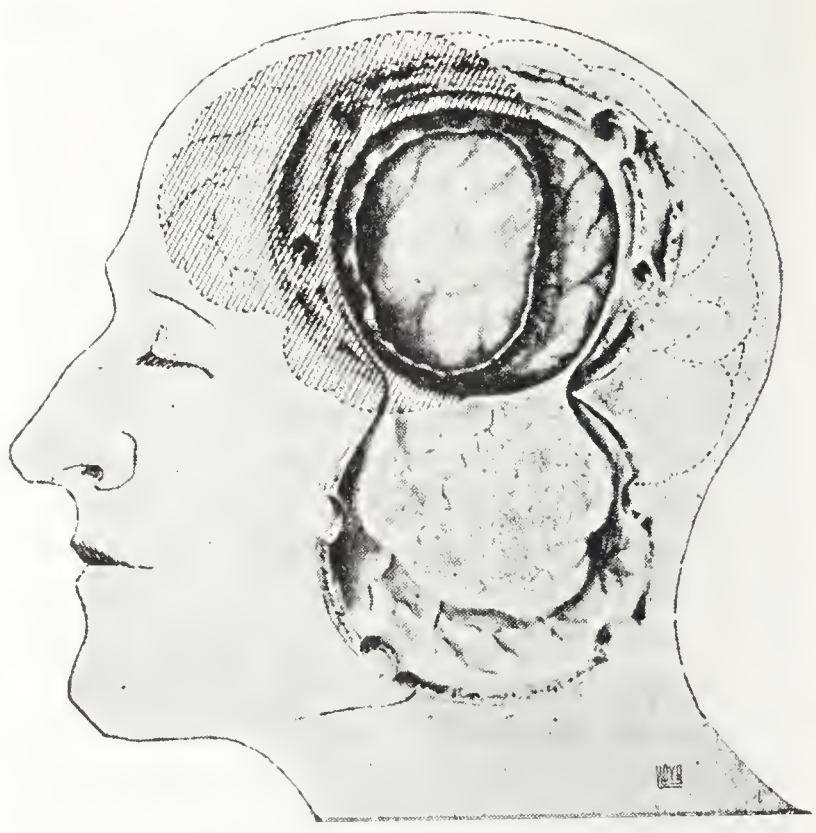

Illustration 8.

Schematic appearance of the hematoma after the outer membrane had been opened and the contents of the sac evacuated. The inner neomembrane can be seen to be of a light greenish tinge and is translucent. The underlying convolutions of the brain can be seen shining through. This membrane is freely movable over the underlying brain. The greenish tinge is largely due to the transmitted color of the brain which has a decided yellowish tinge underlying the hematoma. The size and location of the entire hematoma is indicated by the shaded area. Reprinted from a paper by Carl W. Rand published in the Archives of Surgery vol. 14, pp. 1136-1165. 1927.

5. Primary intra-dural haemorrhage, resulting in a vascularized reaction on the inner surface of the dura. Repeated haemorrhages may then occur from the thin-walled blood spaces of this newly-formed sub-dural membrane.

There are two clinical groups: the acute and chronic.

Acute Sub-dural Haematoma.

Sub-dural blood in varying amounts is present, with any head injury which causes superficial bruising of the brain and tearing of the arachnoid. During the first few days surgical intervention is seldom indicated as the associated brain damage is of more importance than the sub-dural blood, and these patients should be treated expectantly at

this stage. After a few days, when bleeding has presumably stopped surgical intervention is indicated on a few patients who are not progressing favourably. The mental faculties remain clouded and headache is severe, the cerebro-spinal fluid pressure is high and choked discs may develop. There may be some lateralizing weakness. An exploratory burr hole is indicated, on both sides. If sub-dural blood is disclosed it is usually a relatively soft clot mixed with cerebro-spinal fluid. By enlarging the burr hole it is then possible to wash and suck out the blood. In these acute cases the blood is not enclosed in the new-formed membrane which is so characteristic of chronic sub-dural haematoma. The results following operation in the acute cases are satisfactory provided operation is not performed until the acute phase of the brain injury has subsided. In my experience the successful cases have been operated upon between three and ten days after the accident.

Chronic Sub-dural Haematoma.

There are two points to remember especially about this condition: First, it is produced by a relatively trivial injury which tears one or more of the unsupported sub-dural veins as they leave the arachnoid to enter the longitudinal sinus. Second, symptoms and signs are not very definite until a period of weeks or even months has passed.

The initial bleeding probably covers the hemisphere with a thin clot. In a few weeks this clot becomes surmounted by a new-formed thin membrane which is attached to the dura but not the arachnoid. As the clot breaks down in this sac, fluid is attracted by osmotic pressure and it gradually increases in size, so that at the end of six or eight weeks there is typically a lesion which covers most of the hemisphere and is one inch in thickness at its greatest depth. The lesion is frequently bi-lateral.

A summation of experience with these lesions produces the following composite picture:

"A man aged fifty years slips on the ice and falls, striking the occiput. He gets to his feet, slightly dazed for a minute, following which he has pain in the head for a few hours, but this is not severe enough to warrant his going to bed. Thereafter, he feels quite well and dismisses the accident from his mind. Four weeks later he begins to have headache, which increases in severity. The relatives then notice changes in his behavior, accompanied by mental confusion and increasing somnolence. These signs and symptoms show gradual progression and finally the patient is admitted to the hospital three months after the accident in a stuporous condition. On examination, the patient is aroused with difficulty. He is dehydrated." (Gardner).[1]

The neurological signs are frequently vague and conflicting, typically, however, there is some hemi-paresis and choking of the discs. If an eye-field defect is present it is strong or perhaps definite evidence in favour of an infiltrating tumour rather than a sub-dural haematoma.

Operation.

The diagnosis is confirmed by making a burr hole over the upper temporal region opening the dura and exposing the outer membrane of the clot. The bone and dural opening are then enlarged to three cm. in diameter. The outer membrane is opened and the contents of the haematoma sac are sucked and washed out. Drainage is necessary for twenty-four or forty-eight hours to permit expansion of the depressed brain. Both sides should be explored.

The results following operation on these chronic cases are excellent. In our series there have been two deaths in thirty-six cases. The surviving patients are practically all well and at work.

6B. Sub-dural Hydroma.—Dr. Naffziger[2] of San Francisco, drew the attention of the medical profession to this pathological condition in 1924. The trauma produced a tear in the arach-

noid, permitting the cerebro-spinal fluid to escape and pocket in the sub-dural space. There are two groups: acute and chronic. The signs and symptoms are similar to those described under acute and chronic sub-dural haematoma and it is impossible to differentiate between the two conditions. Treatment is the same as that for sub-dural haematoma. In my experience this pathological condition is decidedly rare.

7B. Localized Intracerebral Haemorrhage.—Two or three days after an injury and presumably after bleeding has stopped one may occasionally consider exploring a patient who is not progressing satisfactorily and who has some definite lateralizing sign such as a hemiparesis. For the most part, however, these patients have been operated upon several weeks after an injury, the signs gradually becoming definite because of the fluid content of the haemorrhage increasing from osmotic pressure. It is hardly possible to differentiate such rare cases from sub-dural haematoma or tumour.

C. **The Importance of Adequate Records**—The importance of adequate records cannot be over emphasized. It is the house-surgeon's duty to make a long hand note while his observations are fresh in his mind. The hour and minute of this note should be accurately timed and at least cover the following points:

1. Time of accident, type of injury, i.e., a sharp instrument or corner likely to cause a puncture wound or depressed fracture; a blunt instrument or pavement likely to cause widespread damage and contra-coup laceration. This is especially true when the blow is on the back of the head, and taken into consideration with other findings, such as blood in the cerebro-spinal fluid, and possibly loss of smell, often enables one to make a very accurate diagnosis of laceration of one or other fronto-temporal areas of the brain.

2. State of consciousness, i.e., rational, restless and talking at random, restless and not talking, responding to painful stimuli, not responding to painful stimuli, etc.

3. Respirations, pulse, and blood-pressure.

4. Pupils.—It is highly important to know if one pupil was dilated within a few minutes of the accident (immediate injury to the third nerve or its nucleus) or became dilated at some later date (not immediate injury to the nerve, but probably due to a space-taking intracranial haemorrhage).

5. A comparison of active movement of the arms and legs and the reflexes, at the elbows, knees and on plantar stimulation.

6. Information obtained from a lumbar puncture. (See Lumbar Puncture).

7. Information obtained from x-rays. (See x-rays).

Subsequent notes covering these points are indicated at intervals, possibly every hour or so or even oftener depending on the progression of signs and symptoms. These notes should be carefully timed so that they can be interpreted in conjunction with a special half-hour pulse, respiration and temperature record kept by the nursing service. In many cases all that is required is a good preliminary note, short progress notes and an adequately complete neurological examination on discharge. Apart from diagnosis and treatment adequate records are of great importance if the case becomes a medico-legal problem. (See Medico-Legal).

D. **Lumbar Puncture.** — Lumbar puncture is of great value, as it enables one to measure intracranial pressure and the amount of blood in the cerebro-spinal fluid. In some clinics it is considered to be a very valuable therapeutic procedure; we doubt if it is ever a lifesaving measure and feel that under certain circumstances the withdrawal of large amounts of cerebro-spinal fluid may be harmful.

1. *As a Diagnostic Measure.*

The patient must be quiet and without elevation of the head to estimate

accurately the cerebro-spinal fluid pressure. The *Ayes manometer which records the height to which the cerebro-spinal fluid rises in a small bore glass cylinder is convenient to sterilize, inexpensive and simple to use. The upper limit of normal pressure is 180 mm. The reading is a reliable index of intracranial pressure, if there is no block in the cerebro-spinal fluid pathway about the cord from a fracture of the spine or blood clot at the foramen magnum. An estimation of pressure based on the rate at which cerebro-spinal fluid drips from a lumbar puncture needle is unreliable. After measuring the pressure from two to four c.cms. of fluid are collected in two tubes. The fluid may be clear and without blood, heavily loaded with blood or cloudy when there is a small amount of blood. When there is a small amount of blood the question arises as to whether it is due to trauma from the puncture, if so the second sample should contain less blood. A more reliable test is to centrifuge the sample, the supernatent fluid will show a yellow tinge from breaking down corpuscles, if blood has been present in the cerebro-spinal fluid for more than a few hours. The fluid loses this yellow colour about seven or eight days after all bleeding has stopped.

In general it can be stated that a large amount of blood indicates a severe bruising and laceration of the brain and consequently a serious immediate prognosis and if the patient survives a precarious ultimate prognosis. If a patient is unconscious from some unknown cause it is of the utmost diagnostic importance to know the pressure and cell content of the cerebro-spinal fluid. (See Differential Diagnosis).

2. *As a Therapeutic Measure*

If the diagnostic puncture has demonstrated blood in the fluid one should consider the daily removal of 15 or 20 cc, commencing on the third or fourth day, that is, at a time when presumably all bleeding has stopped. The fluid is removed slowly and frequently makes the patient more comfortable by relieving headache, stiffness of the neck and diminishing fever. Breaking down blood in the cerebro-spinal fluid may produce a temperature of 102 for a week or more. It is unusual to carry on with these therapeutic punctures for more than a few days. We are inclined to do therapeutic punctures much less frequently than formerly and are quite content to carry on without them if the patient is comfortable and making satisfactory clinical progress. The generally accepted contra-indications to lumbar puncture are as follows:

1. Shock.

2. Marked restlessness. This applies especially to the therapeutic puncture when more harm than good is done by trying to hold a fighting patient. A diagnostic puncture may have to be done on a restless patient but only when it is really important to know the pressure or amount of blood in the spinal fluid, i.e. in a semi-conscious patient from some unknown cause or in a suspected extra-dural haemorrhage.

3. The withdrawal of large amounts of fluid shortly after the accident may produce fresh haemorrhage or upset the purposeful physiological reactions to injury.

4. If unconsciousness is becoming more marked and if the pressure is rising, lumbar puncture should only be used as a therapeutic measure after exploratory burr holes have ruled out some space-taking lesion, and demonstrated a general oedema. Even then the fluid should be removed cautiously and only repeated if it results in a decided clinical improvement. In such a situation hypertonic glucose is probably more clearly indicated. The removal of a large amount of fluid in the presence of a space-taking lesion is definitely contra-indicated as it may rapidly change the patient to a hopeless operative risk.

E. **X-ray Examination.**—X-ray examination is done for two reasons:

1. Information may be obtained which is of value from the standpoint

*This manometer may be purchased at Toronto Instrument Houses at $8.50.

of treatment. A depressed fracture is a definite indication for operation. A linear fracture crossing the middle meningeal or its branches indicates the possibility of extra-dural haemorrhage.

2. Medico-legal (See Medico-legal).

X-rays should only be taken after a patient has recovered from shock, in many cases it is delayed for days. If there is suspicion of a depressed fracture plates should be obtained as soon as possible. It is important to appreciate that a linear fracture is difficult to see if the side on which there is a fracture is not next the plate, when the x-ray is made. As a routine stereoscopic plates are made from the anterior, right and left positions. In the medico-legal case special plates to show fracture of the base may be advisable.

F. **Cerebro-Spinal Fluid Leak from the Ear or Naso-Pharynx.**—A leak of cerebro-spinal fluid is accompanied at all times by great danger of meningitis. The outer part of the ear canal and surrounding parts are kept clean and a pledget of cotton soaked in 65% alcohol is placed in the ear and changed every few hours. The canal must not be syringed or have hydrogen peroxide put in it. The patient is cautioned against violent blowing of the nose when there is a leak into the naso-pharynx.

Fortunately most leaks stop within a few days. In the occasional case where the leak persists for weeks, consideration should be given to the possibility of stopping it by an intracranial exposure and the application of a patch of fascia at the leaking point. Occasionally when the fracture has passed into the frontal or ethmoid sinuses an x-ray will show air in the intracranial cavity.

G. **Length of Time in Bed and Advice on Discharge.**—Some writers advocate prolonged periods of absolute rest in bed. In practice and in theory there are objections to this. The patient who is dazed, or unconscious for only a few minutes, can get up the following day and if he is feeling well can go on with his business. In the more seriously injured group, frequent active changing of position is encouraged as an aid to cerebral circulation. The patient may sit up out of bed if he wishes to, usually this is preceded by a period in bed when the head is well raised; the patient can be encouraged to sleep in this position and so accustom and retrain the circulation to function adequately in the upright position. When a horizontal position is maintained for a prolonged time, the circulation fails to adjust itself rapidly to changed position and undoubtedly considerable post-traumatic headache and dizziness are due to inadequate circulatory response. In brief then, even the seriously injured group may be allowed up as soon as they feel equal to it.

When a patient is discharged, it is very important to impress on him that eventually recovery will be complete or nearly so. There may be a period of months when there is headache, dizziness and general lack of strength and initiative; during this time the patient must be encouraged and reassurred. It is quite possible that somebody has told him that his brain has been injured, and that he will never be well. If however, he can be persuaded to carry on, it is almost certain that in a year or two all symptoms will have disappeared. There is no group of patients more prone to develop functional complaints. If part time work cannot be arranged, a return to full duty should be postponed until the patient has recovered to the point where he is not likely to have to stop work, a bad blow to his morale. Many patients stop work because they feel that they are doing themselves harm, because of some increase in symptoms; usually this is not so, if possible they should accept the symptoms and continue work for in time improvement will take place.

In compensation and medico-legal cases, the problem of getting a patient to work is a much more difficult one. In general, work will not increase any existing pathological condition and the sooner an individual gets back to a job and stays at it the better.

Most patients should be given de-

finite future appointments every month or so to give them a chance to explain their symptoms, and also give the doctor an opportunity to satisfy himself that there has been no development of some such lesion as a chronic sub-dural haematoma or hydroma.

H. **The Treatment of Post-Traumatic Headache and Dizziness.**—The writer has already indicated that these symptoms are more likely to be severe and prolonged in the patient who has been kept flat on his back for a prolonged period. This opinion, at variance with that of many writers, was crystallized by an experience with a patient who had been kept flat in bed for many weeks. When this patient stood up he became very dizzy because his blood pressure dropped to almost nothing. He was cured in a few months by sleeping with the head well raised and by being up and carrying out exercises which involved stooping and rapid change of position.

In most patients these symptoms usually improve as the months go by and will have entirely disappeared in a year or two at the most. In a few improvement takes place and active treatment is indicated. This involves careful neurological examination and history taking. Possibly only re-assurance is necessary especially if the history brings out the fact that the patient has been told by some well meaning friend that his brain has been damaged.

An increase in the cerebro-spinal fluid pressure or choking of the discs, indicates a sub-dural haematoma or hydroma and must be dealt with by operation. Very occasionally one encounters a case with a high cerebro-spinal pressure from a persistent oedema of the brain. Only time will rectify such a condition, although lumbar puncture and 50 cc. of 50% glucose administered intravenously may hasten recovery. A space-taking lesion must of course be first ruled out.

In other cases when the pressure is normal and there is no indication of the lesions just mentioned one considers the advisability of an encephalogram or a burr hole and dural opening combined with a lumbar puncture. Either one of these procedures help certain patients, presumably by breaking down painful adhesions. Penfield[3] has been the chief advocate of this form of therapy. Our most striking results have been obtained by the combined dural opening and lumbar puncture method. It also has the advantage of being easier on the patient and permits the operator to rule out sub-dural haematoma. The best results are obtained on patients with unilateral and fairly well localized headache.

When a fracture has injured the inner ear, the patient may have vertigo comparable to Ménière's syndrome. In selected cases section of the vestibular portion of the eight nerve will give good results.

I. **Prognosis.**—In general children and young people recover without disability following a brain injury. On the contrary, individuals over fifty frequently do badly; in part because the cerebral pathways are more definitely fixed, but also no doubt because a certain zest in life is gone and cerebral and physical activities are diminishing.

Epilepsy of varying degree occurs in a high percentage of cases, (20% to 40%), following a depressed fracture which produces sufficient local injury to cause considerable scar formation. Usually the seizures do not occur for some years after the injury. In patients without a depressed fracture the incidence is much lower, possibly 5%. (The normal incidence of epilepsy in the population is ½ of 1%).

Massive injuries may produce a permanent hemiparesis, aphasia or marked mental deterioration, but these are rare, largely because most of these patients die. When there is mental deterioration and poor social adjustment, it is frequently an exaggeration of a pre-existing condition.

Certain cranial nerves are especially subject to injury:

(a) Contre-coup frontal bruising may injure the olfactory nerves and

cause a permanent loss of smell and ability to appreciate flavours.

(b) Permanent loss of function of the optic nerve may result from injury at the optic foramen.

(c) Ophthalmoplegia of varying degree may result from injury to the third nerve or its nucleus. Unless there is evidence of recovery within six months, the paralysis will be permanent. The patient in time accustoms himself to the disability by focusing with the good eye alone.

(d) Fracture through the petrous bone may injure the facial and auditory nerves. If there is not definite evidence of recovery in six months some form of repair of the facial nerve should be considered.

J. **Medico-Legal.** — Adequate records are of the utmost value and will save the doctor many unhappy moments in the witness box. In particular an accurate knowledge of the length and degree of unconsciousness, blood in the cerebro-spinal fluid, cranial nerve palsies, unilateral weakness and x-rays are required.

A doctor should guard his patients against too early settlement. On the other hand when the case has progressed to a point where a reasonable estimate regarding disability and prognosis can be made—settlement is highly desirable. Undoubtedly an unsettled legal claim is very detrimental to the patient's recovery. From the standpoint of health it is better to have a claim settled quickly and for a smaller sum, than have it drag on for a year or more. Unfortunately some insurance companies are not particularly co-operative with the patient and his doctors. In estimating disability it is wise to have the additional opinion of one or more consultants.

K. **Differential Diagnosis in the Unconscious Patient with a Bruise or Cut on the Head.**

1. The individual with the smell of alcohol in his breath. These are troublesome cases and should be kept in hospital over night. If the patient is co-operative or quiet, a lumbar puncture is of great value—blood in the cerebro-spinal fluid definitely indicates cerebral trauma. If there is no blood, and especially if there is oedema over the temporal region, close watch should be kept for the signs and symptoms of a middle meningeal.

2 The epileptic. When there is a history of epilepsy it is probably just another fit. Again lumbar puncture is of value, if there is not a rapid return to consciousness.

3. When there is no definite history of an accident, the patient may have fallen because of a spontaneous intracranial haemorrhage. A large amount of blood in the cerebro-spinal fluid suggests such a diagnosis, especially if there is a profound hemiplegia.

4. Choked discs during the first few hours in any cranial trauma suspect, indicate a pre-existing space-taking intracranial lesion.

5. Haemorrhage from a ruptured liver or other organ may be severe enough to produce unconsciousness.

6. Relatively moderate head trauma may produce unconsciousness in patients with pre-existing cardio-vascular renal disease. In older people an N.P.N. and urine examination are especially important.

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COMMON SENSE AND CLEAR THINKING AMONG INVESTIGATORS

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Most scientific facts are accepted on faith. We trust the frequently dogmatic conclusions of authorities in all but our own narrow field of knowledge. We know that differences of opinion exist but very few are capable of examining closely the data in the vast realms of human knowledge. First hand evidence is known only to the specialist. How are we to know whom we may trust? This has puzzled and always will puzzle mankind. It requires a certain amount of careful training to enable us to tell the quack from the true scientist, the demagogue from the statesman, the philosopher from the charlatan. It is not always easy. The chief purpose of school and university discipline is to indicate in the most direct way the course taken by clear thinkers in their forward march. It is permissible on occasion to suggest the probabilities or possibilities for the future but this must be done humbly and never dogmatically.

In any field of endeavour the sensible approach is first to know what has been done, how it has been done and how well the accepted facts have been supported by reliable experiment. This is the historical approach.

History by derivation simply means to learn by inquiry. The more such an inquiry is punctuated by the adverb "why," and the keener the student is to answer accurately this ever recurring question, the more profit will be gained and the more intelligent will be his approach to his subject.

Perhaps the most difficult thing in thus delving into the past is to learn just what facts were available at any one time which stimulated the searcher to take the next forward step. It is so very easy for us, armed with a fuller knowledge, to feel how smart we are and how stupid they were. The direct questions we should ask ourselves are, "What would I have done?" "What would I have thought?" having as my background only the then accepted "facts" and beliefs. "Facts," however are not as rigid as we would like them to be. Theories are only explanations based on analogy with concepts or "facts" already widely accepted. Ultimate explanation has not and never will be reached. "Common Sense," as one of our visiting lecturers recently said, "is simply the sense common to the mass of the people at any one time," and he added, "Horse Sense is the sense we would expect from a horse."

Let us then enquire how we have arrived where we are today in our knowledge of bacteriology. Life and death have always loomed large among the things which naturally interest the inquisitive mind of man. Despite all our heaped up knowledge these two events are still as mysterious as they have ever been. "Into this universe. . . . and out of it, like wind along the waste, we know not whither willy-nilly blowing," sings the poet. To save his sanity man has steered his course free from these ultimate problems of the beginning and the end of life. But what about early deaths—deaths before the allotted span of life has been fulfilled? Explanation of deaths from war, accidents or starvation seemed easy—the mechanism was obviously destroyed or rendered useless by loss or lack of working material. This did not seem sufficient, however, to explain disease nor the terrifying experiences of the great plagues. Here nothing was obvious except the impressive and awful facts. A theory of some kind had to be evolved —this being a fundamental characteristic of man's mind. Those who accepted demons as factual entities apart from man naturally suspected or firmly believed that these were the cause. This sufficed for long years. Measures were

devised by "medicine men"—the priests of the day—to exorcise or sometimes to pacify these evil spirits. An occasional accidental autopsy divulged unexplained cavities in the bodies of the dead—the dwelling places of the demons—which helped to strengthen such beliefs. Others taking as truth the direct interference of the gods in the lives of man were satisfied that these phenomena represented punishment by these unseen beings for the breaking of religious laws. Sacrifices and lustrations were widely used to appease the gods. Today the tendency is to accept disease as due to not obeying the laws of health, known or still unknown.

Along with these hypotheses but in part independent of them there arose a number of beliefs based on more or less accurate observation. The predominance of certain diseases among people living near swamps and in damp climates had been noted by the Greeks and Romans and this led to the "Miasmatic Theory." A more remarkable observation was the association of night air and Malaria (Mala Aria—Italian for bad air), which many years later was confirmed when it was discovered that the female mosquito, the carrier of the malarial protozoan, bites at night. Shakespeare speaks of Brutus leaving his bed, "to dare the vile contagion of the night and tempt the rheumy unpurged air." Cosmo-telluric postulations based largely on chance coincidence of earthquakes, comets in the skies or other natural phenomena, but sometimes on climatic and seasonal differences in disease incidence were widespread. Coincidence is a big factor in the success of quackery today.

The "Theory of Contagion" is very old. There are many references to it in the Bible and other early writings. Practical applications of this conception are seen in the regulations against lepers, the quarantine laws of Venice in 1403 and numerous other methods adopted to check the spread of disease. The nature of the thing transferred was quite unknown and the theory included the idea of miasmas surrounding the ill person in some mysterious way, but despite the necessarily hazy and diffuse views it was from this that the modern theory eventually developed after the fullness of time made possible more exact observations.

Keen as were the correlations between observed fact and philosophical reasoning by Fracastorius (1478-1558) in his "De Contagione" (1546), in which he likened contagion to "the spreading corruption seen in grapes," his views were held to be purely speculative and made no permanent impress on either medicine or science. He believed there were seeds of contagion invisibly small which could multiply and propagate their like; the diseased tissues gave rise to these seeds which could "convey the infection to others whether the same causes or dispositions be acting in those others or not." He came astoundingly close to our modern beliefs, but what his views were about the independent living nature of his "seminaria" or whether they simply acted as vehicles for conveying the "essence" of the contagion are not quite clear.

Man was penetrating the unknown. Copernicus had discovered the revolution of the planets around the sun, Columbus had broadened our knowledge of the earth and Fracastorious had taken a first step into the world of little things. Slowly knowledge grew. Men like Galileo began to peer into the heavens through telescopes. Shakespeare crystallized the beauty and the wonder of man's mind in literature, and here and there crude microscopes were being used and the marvels of an unseen world began to be revealed. The itch-mite was found in 1657, a living creature in the skin of man.

Kircher (1602-1680), a Jesuit Priest, poured out his uncritical speculations and having seen under his microscope strange looking groups of red cells in the blood of a man dead from plague expressed the belief in 1658 that they were worms and the cause of the disease. His observations were quite wrong, his microscope could not have shown

the tiny plague bacillus but he boldly postulated the doctrine of "Contagium Animatum" in 1671 believing these small living creatures had come into existence since the Ark. Even thus were the thoughts of man being prepared for what was still to come.

During this same period there lived in the little town of Deft, Holland, Antony van Leeuwenhoek (1632-1723), a man who did not speculate but who simply observed, and recorded with meticulous care all the things he saw through his wonderful little biconvex lenses—magnifying-glasses mounted in a metal frame with mechanical parts to move the objects towards the lens—the whole scarcely larger than a visiting card. The Royal Society had recently (1662) been founded in London, and it has been suggested that this group of keenly inquisitive minds might never have come together had they not been driven to seek comfort away from their cold homes at a warm and cheerful Inn. To them Leeuwenhoek sent the reports of his findings. In the famous letter of October 9, 1676, he first described bacteria in water, and in 1683 in material from between his teeth he noted the first parasitic forms.

Leeuwenhoek's microscope, actual size.

Thus bacteria first appeared to man, but there were no suggestions at this time as to their significance in the scheme of life and certainly none in connection with disease. However, a country physician in Kent, Thomas Fuller (1654-1734) wrote a fascinating book at the age of seventy-six called Exanthematologia (1730). He had heard of Kircher's doctrine and Leeuwenhoek's discoveries and recorded the opinion "that animalcules have been the cause of malignant pestilential fevers" and that "these differ in essence and symptoms, according to the nature and venoms of those creatures."

Microscopes became more powerful. Numerous bacteria and other microscopic living forms were discovered. Linnaeus in 1767 classified these with spermatozoa and pollens in a group called "Chaos infusorium." Theories multiplied. Living contagion and specificity were again suggested. Morphological classifications were published. A fungus disease of silkworms was recorded. The agents of favus and thrush were seen. Wild speculation without scientific proof was the order of the day as we approach the time of Pasteur. The stream of knowledge was fed from many sides. There were obstructions which had to be overcome. Often these obstructions helped to strengthen the force of the ever increasing scientific facts, and when after long labour the flood finally broke the torrent swept away much valuable experience and reliable observations which after long years had to be rebuilded so that the river might flow full and strong but more usefully because controlled.

I have already said that man was interested in birth and death. He was also, and still is, deeply concerned with the origin of life. Here again theories and beliefs have been founded on "facts," and these in turn have been determined by observation at first rough and superficial but gradually becoming more and more delicate and acute. It was widely held that living things originated from dead or lifeless material. In mythology dragon's teeth grew into warriors. The centaurs, creatures half man, half horse, became part of the people's folklore because of careless observation by the wandering Greeks when first they saw Arabs on horseback. Aristotle believed frogs came into being from the slime of the river Nile. Swarms of bees in the carcases of dead animals and hundreds of similar experiences kept the idea alive. A great chemist, Van Helmont, in 1652, only a few years before Leeuwenhoek's beautiful observations

gave his celebrated recipe—dirty linen in a receptacle and a little cheese would surely create mice. He was surprised, however, that these were adults.

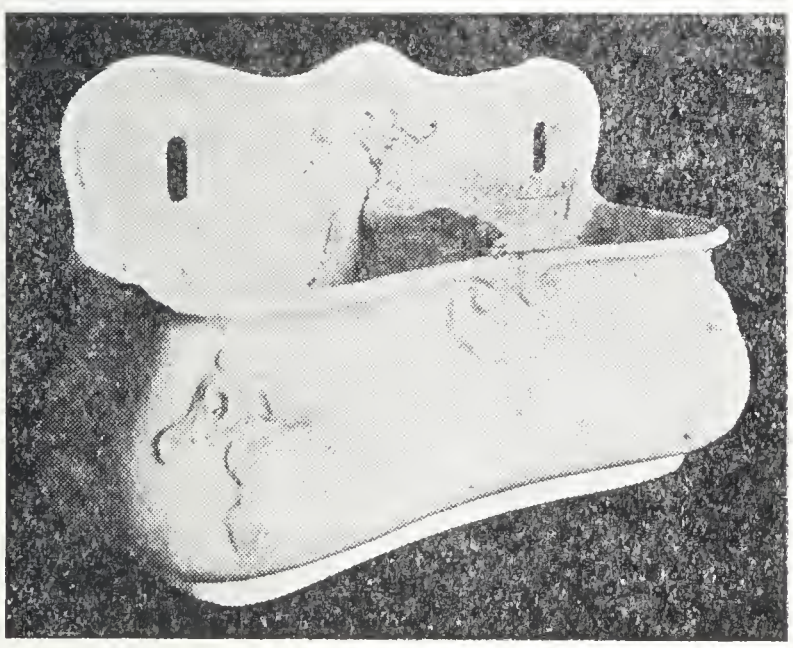
Francesco Redi (1626-1698) the father of Zoology, did the first experiment on this problem in 1668, if we disregard van Helmont's. He proved that maggots were not generated in decaying meat. He put meat in two jars, covering one with a fine gauze, and noticed that flies laid their eggs in the open jar and these grew into maggots. Simple indeed, but each forward step seems equally simple to the scientific searcher. Redi, however, was not able to observe the story of the worms found in galls of trees and thought there might be a life-principle in the living tree which could create them.

When the microscopic world was revealed the age-old controversy was revived, and although Leeuwenhoek himself believed his "little animals" came from seeds or germs in the air nearly everyone was sure that the actual creation of life was being revealed. Needham (1713-1781), an English Jesuit and physicist, was among the most active supporters of "Spontaneous Generation" and carried out numerous experiments to prove its truth. He philosophized that vitality is an indestructible quality and that the theory was logical since "organic molecules can enter into the most diverse combinations." Then he heated mutton broth, put it in a phial closed with a cork covered with mastic and found in a few days that it was swarming with living things. Thus he "proved" a vegetative force capable of creating life from "dead" materials. These claims came to the attention of a really great mind. Spallanzani (1729-1799) repeated these experiments but with infinitely greater care. He found if the glass containers were well heated before the infusion was added, the air removed by an air pump and the flasks hermetically sealed, then no life appeared. Needham replied that the prolonged heating had injured the vegetative force and that air was needed to vivify it. These criticisms were answered, but since the problem was largely academic relatively little general interest was aroused, and most of the leading naturalists believed in spontaneous generation until well into the nineteenth century.

A practical application of these results was made by Appert in 1810, for the preservation of food, but he does not mention Spallanzani's work. He is the founder of the canning industry. Oxygen had been discovered in 1772 (Priestly), its relation to respiration noted in 1775 (Lavoisier), and Gay-Lussac tested these bottles of Appert's and found they did not contain oxygen. He therefore postulated that oxygen is needed to start fermentation but not for its continuance. A series of experiments followed which showed: that air after bubbling through strong acids (Schulze, 1836); or after heating and still able to support respiration in frogs (Schwann 1837); and finally after filtering through cotton (Schroeder and von Dusch, 1853), was unable to initiate life in infusions which had been sufficiently heated. Thus briefly we have followed another stream which freshened by the genius of Pasteur poured into the one previously outlined to help form the strong river of the "Germ Theory of Disease." There were still other contributories. Some started as mere suggestions, such as Robert Boyle saying in 1663, "that he, that thoroughly understands the nature of ferments and fermentations shall probably be much better able than he, that ignores them, to give a fair account of divers phenomena of several diseases." The theories explaining fermentation and putrefaction were scattered over the watersheds of knowledge, many dried up near their source, others formed swamps, some trickled on, often underground, to form a sizeable stream. Thus fermentation was postulated as: "an internal commotion of the particles" (Thomas Willis, 1659); or "a purely chemical process" (vital processes having been demoded with the synthesis of organic substances (1828);

or caused by a "catalytic principle" (Berzelius, 1836); or due to the chemical instability of non-living substances called "ferments" (Liebig, 1839, and until his death, 1873).

Two other life-giving rivers had also appeared. One of these owed its origin to the translation into practice of a countryside tradition in England that dairy maids who had had cowpox did not take smallpox. Jenner (1749-1823) told this story in 1778 to John Hunter (1728-1793) and wondered if it might be true. Hunter replied: "Don't think, try; be patient, be accurate." Jenner acted. The result was that he proved the truth of the tale in 1796 and established vaccination against smallpox, one of the greatest prophylactic measures ever devised by man. Hunter did not live to see the fulfillment of this scientific triumph, having died three years before.



Semmelweiss basin used for disinfecting hands with chlorine.

The other river developed from the ancient indefinite theory of contagion. Semmelweiss (1818-1865), the "saviour of mothers," believed the cause of puerperal fever to be a "decomposed animal organic material" from any source of disease. A man in the pathology service died as the result of a wound infected at an autopsy on a puerperal fever case, and Semmelweiss seeing changes in his body similar to those in the female cases realized that the causative agent was not therefore specific for "Child-bed Fever." Students coming from autopsies apparently transmitted this agent to the puerperal women and Semmelweiss laid the foundation of modern obstetrical prophylaxis when he instituted chlorine disinfection of the hands (1847). The views as to the causative factors of this dread disease of mothers were at this period numerous and included "Genius epidemicus," "Miasmas," "Contagion" (as a specific virus originating during the disease), or it arose from suppression of the lochia, or as a result of the physiological upset associated with the production of milk, or due to a state of unstable equilibrium such as a change in the blood.

As Shakespeare had gathered together the scattered and uncertain tendencies of literary strivings in the days of Elizabeth and by his mighty genius created a standard for all time, so in the land of science by the magic of his clear and penetrating mind, Pasteur gave scientific force to all these little streams of thought and practice, and has fundamentally changed our outlook on life and made possible a safer and happier existence. Two great dangers—famine and infectious disease—have been brought under measurable control, and the biological scheme of life has become clarified as a result of his studies. To appreciate what Pasteur did requires not a superficial but a detailed knowledge of his work. Duclaux's book, "Pasteur, The History of a Mind," gives some insight into the logic of his thoughts.

Louis Pasteur (1822-1895) was a great French chemist and founded, when under thirty, Stereochemistry—the chemistry dealing with the structural form of chemical compounds. He noticed macroscopically visible differences in the crystal forms of certain tartrates and found that these differences persisted in the molecules when in solution, in that they turned the direction of polarized light either to the right or to the left. A mixture of the right and left salts showed no apparent change in the light—the combined ef-

fect was a neutralization. Working with such a mixture he found one day that it had changed—the right tartrate had disappeared. Why? Because living germs had fallen into his solution and by their activity had broken down the salt. This opened the way to the problems of fermentation and spontaneous generation which, after long and accurate experiment and with keen interpretations of all results, he finally solved. The fuller application of the basic facts established by Pasteur has led to: the modern methods of food preservation and the elimination of famines; the growth of organic chemistry; the place of bacteria in the cycle of life through their function in breaking down complicated compounds of dead organic materials and setting free simpler chemicals, making them available for use by new growing plants; and finally to real knowledge of the cause, prevention and cure of infectious diseases. In all of these developments Pasteur was the leader and did an almost unbelievable amount of work.

"It is rare that the human mind sees simply," said Duclaux. Experiment, freed from concepts and formulas, brings simplification. Pasteur experimented, allowing each step to lead him to the next. In 1865 Lister, groping for an explanation of post-operative infections, heard of Pasteur's results in solving the riddle of fermentation, applied the ideas to surgery and thus founded antiseptic and aseptic surgery. In this same year Pasteur began the study of Silk Worm Disease. In six years he found the causative agent, the mode of transmission and a practical method of controlling the disease, and thus saved a great industry. Students of medicine clamouring for instruction about germs and their place in infectious diseases were given his book, "The Diseases of Silk Worms," as a text. It is, indeed, a model for the principles of scientific control of disease. Following this and in spite of a paralytic stroke in 1868, Pasteur with the touch of genius clarified the work of Robert Koch and established the etiology of Anthrax not as a virus but as a living, visible germ. He developed the method of protective vaccination against Anthrax, giving full credit for the idea to Jenner's great work of 1798 against smallpox, discovered and showed the significance of anaerobic bacteria in war wounds and a logical technique for treatment (1878) which waited for practical application until the second year of the Great War. He entered into the problem of the virus disease Rabies, and refusing to be diverted into a search after the causative agent, discovered the life saving treatment which won for him the hearts of mankind in all parts of the world.

The imagination and lucidity of thought of Pasteur, the sound, practical mind of Lister, the systematic, illuminated but less inspired intellect of Koch formed the triple foundation which has taken the Germ Theory of Disease out of the realms of academic speculation and has made of it the principle which has revolutionized not only medicine and surgery but also chemistry, biology, industry, and has changed all our mode of life.

Unfortunately the evidence coming from every side was so convincing that it swept all before it. The simple logic of Pasteur's unbiased experiments which he had instilled into science was all but lost in the rush of new confirmations. It has therefore needed the steadying influence of time and experience to curb the minds of men and to make more effective the accumulated facts. If the river of knowledge is to hold its strength it must still be fed by innumerable streams rising in laboratories everywhere and controlled by practical experience. The next great advance will come when a new Pasteur is found to correlate the gathering information and to foresee the new course which science will follow in the future. Common sense is changing with the times but there are many people still following the will-o'-the-wisp of antiquated theories. Clear thinking is extremely rare but it alone can guide investigators on their new voyages into the unknown.

MENORRHAGIA AND METRORRHAGIA

By MELVILLE C. WATSON, M.B.

The investigation of the cause of excessive, or irregular bleeding from the reproductive tract in women is not essentially different from the investigation of internal bleeding from any other source in the body. Here, as elsewhere, it is first necessary to locate the site of the origin of the bleeding. One must next determine why bleeding is a symptom of the presence of that particular lesion. Successful treatment of the symptom or the cause of the symptom, depends entirely on the accuracy of the information which the clinician can obtain concerning these two facts.

No one should attempt to treat prolonged excessive menstrual flow, or irregular vaginal bleeding between periods without having first determined the location of its source. This might appear to be an unnecessary warning, but experience has proven that it is not. In practically every case the patient is complaining of an irregularity in menstrual flow, as it appears at the vaginal orifice. It is not uncommon for vaginal bleeding to be confused with bleeding from the urinary tract, and vice versa, if a complete examination has not been made. Besides the urinary tract, one has to consider lesions of the vagina, the cervix, and the uterus, as being possible sources of the bleeding which appears to the patient at the vaginal orifice.

It has been my practice to begin the examination of the reproductive tract in cases of abnormal bleeding, by a thorough inspection of the external genitals, followed by the use of a vaginal speculum, the size of which is suited to the particular patient; the whole procedure being enhanced by adequate lighting. If the external genitals, the vagina and the cervix, are adequately exposed in a proper light, the location of the source of the haemorrhage, when present in these parts, does not require any exceptional professional skill. Absolute adherence to this simple procedure is a prime necessity if a physician intends to practice this particular branch of his art intelligently.

The common lesions in the vagina and the cervix which cause bleeding are traumatic, simple or malignant ulcerative processes, chancres, polypi and endometrial implants. Eversion of the endocervix after childbirth or miscarriages followed by imperfect epithelialization over the surface is frequently evidenced by irregular bleeding. In the absence of any of these conditions it will be apparent that the free blood is coming from high up in the endocervix, or from the lumen of the uterus, the latter being the more frequent site. If the examination is made during the presence of the symptom, the blood can be seen escaping from the cervical canal.

In dealing with uterine haemorrhage, it is well to avoid the use of the terms menorrhagia and metrorrhagia to indicate a diagnosis. These words were invented to describe symptoms. Nevertheless, they are frequently found on hospital charts along with "idiopathic bleeding" as a final diagnosis. It is true that the diagnosis of the actual cause of uterine bleeding is often difficult. The reason for the difficulty is because the tissues comprising the uterus itself are merely responding to a more remote stimulus. We are now in possession of good evidence, which indicates that nearly all uterine haemorrhages, except those due to destructive ulcerating lesions, can be attributed to disturbances in ovarian function. Uterine bleeding, normally, is a physiological phenomena at the menstrual period. Uterine bleeding is the result of certain microscopic lesions in the endometrium, which in turn are due to a prolonged secretion of oestrin or progestin by the ovaries. Uterine bleeding is a symptom which is frequently

attributed to the presence of myoma, endometrial polypi, endometriosis, and other more obvious lesions in the reproductive tract. However, the simple congestion of the uterus which is associated with these lesions is not sufficient to explain the menstrual excess. Even if we are unable to find an associated state in the endometrium, for which the ovary is responsible, and which contributed to the blood loss, we still have to prove that abnormal ovarian function was not the original cause of the gross lesion with which we are dealing. You are therefore always obliged to consider disease and altered function in the ovaries as you investigate the cause of uterine bleeding.

The ovaries exercise a double control over the uterus. Growth in the tissues comprising the uterus is stimulated, and when the cells of these tissues are sufficiently matured their functional capacity is augmented by ovarian control. The growth stimulating effect, and the excitor influence on uterine muscle, is supplied by the ovarian hormone known as oestrin. The functional capacity of the endometrium is augmented, and a depressor influence over the uterine muscle is supplied, by the ovarian hormone progestin. When the ovarian function is normal and the uterus free from disease, these substances act upon the uterus in a harmonious cyclic fashion to produce the normal menstrual flow from the uterus at fairly regular intervals. This is known as true menstruation and it is always accompanied by a general symptomatic syndrome, which varies in degree, but which always renders the patient conscious of the approaching event.

Any condition which interferes with the harmony which normally exists in the control of the uterus by these two substances, oestrin and progestin, will give rise to one of two symptoms; either total absence of menstrual flow. or menstrual flow which is abnormal in quantity and in the regularity of its appearance in that particular patient. In a previous paper (1) the author has given in detail the microscopic description of the endometrium; (a) during a normal menstrual cycle; (b) as it is maintained by a continuous secretion of oestrin and (c) as it is maintained by a continuous secretion of progestin. It is emphasized in this article, that the symptoms of amenorrhoea, and irregular or regular profuse uterine bleeding are often associated in the same patient where the endometrium is continuously maintained in the proliferative or secretory phase by oestrin and progestin respectively. Endometrial polyp formation is most frequently an end result in an endometrium which has been maintained in an acyclic proliferative phase for some length of time. There now appears to be a very definite association of endometriosis and fibroid formation of the uterus with a slow growing prolonged oestrin or proliferative phase in the endometrium. Future investigations will possibly reveal, that an arrest in the ovarian cycle with a resulting abnormally low continuous production of oestrin is the basic cause of the triad:—endometrial hypertrophy in oestrin phase, endometriosis and fibromyomata. One hesitates to describe the appearance of the ovaries which are associated with these conditions as cystic. The normal ovary is cystic, and there has been in the past far too many of these important organs removed during operation, for no good reason.

Endometrial Hypertrophy in Oestrin Phase

Uterine bleeding is a symptom of this condition which occurs most frequently just prior to the climacteric and less commonly during adolescence or at any time during the reproductive period. In the absence of any other condition at the time of the menopause, both the symptom and the condition are self limited. Therefore one has simply to establish the diagnosis by a biopsy of the endometrium, and if the bleeding is not severe a curettage will frequently hasten the natural cessation. If the

bleeding is severe and there are no complicating conditions, the remaining ovarian tissue which is actively secreting oestrin must be destroyed. This is best accomplished by deep X-ray therapy. Cancer of the body, endometriosis, fibromyomata, polypi or other complicating conditions at the time of the menopause should be treated by the methods laid down in any modern text on gynaecology.

Endometrial hypertrophy with bleeding in the adolescent girl or in women during the reproductive period must necessarily be treated conservatively. One can only speak in general terms where brevity is essential. The past history must be carefully taken to uncover causative factors for the interruption of the ovarian cycle. Chief among these factors are:—infectious diseases—particularly mumps and influenzal types; diets, inadequate in fats and proteins; and a disposition toward endocrine states from which the patient is victimized by similar tendencies in her parents.

FIBROMYOMATA AND ENDOMETRIAL HYPERTROPHY

Uterine bleeding resulting from the combined presence of endometrial hypertrophy and fibromyomata during the reproductive period is a symptom of a state that is difficult to treat conservatively and at the same time successfully. These individuals are usually sterile and this may be the real reason why they seek advice, although they actually complain of vaginal bleeding. Early treatment naturally depends on the extent of the blood loss. If the patient can be treated conservatively from the beginning, the investigation should proceed along lines similar to those adopted in cases presenting endometrial hypertrophy in the oestrin phase which are not complicated by fibromyomata. One must remember that these tumours are often incidental in that they are not the cause of either the bleeding or the sterility. Myomectomy therefore will probably not cure either of the symptoms unless some attempt is made to correct the arrested cycle in the ovary.

ENDOMETRIAL POLYPI AND PEDUNCULATED SUBMUCOUS FIBROIDS

Endometrial polyp formation may be single or multiple. They exist most frequently as an end stage in an endometrium which has been maintained in an unhealthy oestrin phase for a considerable length of time. Endometrial polypi are easily removed by a thorough curettage after which the diagnosis is established. On the other hand the presence of pedunculated fibroid tumours in the uterine lumen is a diagnosis which is frequently missed. There is usually a degree of enlargement of the uterine cavity and of the uterus as a whole in association with pedunculated submucous fibroids. It is difficult to detect the pedunculated mass because the uterine sound and the curette slip around the pedicle freely without giving one any impression of an obstruction in the lumen.

Pedunculated submucous fibromyomata may cause bleeding but they more frequently give rise to a sanguineous, purulent discharge due to degeneration in the tumour itself. If the tumour reaches the internal os, pain becomes an additional symptom because of the expulsive contractions of the uterine musculature. During a diagnostic curettage, to discover the presence of these tumours, one must base the final diagnosis on the following points: enlargement of the uterus, the presence of other fibromyomata, the type of uterine bleeding or discharge, the appearance and the amount of endometrium which is recovered, the size of the uterine cavity and whether or not a pedunculated tumour can be seen, or felt with the curette. If such a tumour is present the amount of endometrium recovered does not correspond with the degree of the bleeding or discharge and the uterine cavity is usually disproportionately large for the size of the uterus.

UTERINE BLEEDING ASSOCIATED WITH OVARIAN TUMOURS

One fairly common form of ovarian neoplasia, the granulosa celled carcinomata, exhibit a strong hyperfeminizing influence, so that in children they bring about precocious development of the secondary sex characteristics with uterine bleeding. During the reproductive period they produce uterine bleeding interrupted by short or long periods of amenorrhoea, while in elderly women they may produce a type of uterine bleeding which is often mistaken for a re-establishment or a prolongation of the normal menstrual function. These tumours may be so small that they are detected with difficulty during a bimanual examination. The treatment is early removal. On account of the rarity of metastasis or recurrence, a conservative attitude should be taken in regard to the healthy ovarian tissue of the unaffected ovary in children and young women. The uterine bleeding is from the endometrium which is maintained in a prolonged oestrin phase by this type of tumour.

Endometrium Maintained in Secretory Phase

It is not uncommon, particularly in the multiparous patients, to find troublesome uterine bleeding coming from an endometrium which shows definite functional or secretory changes. This state in the endometrium is maintained by active lutein tissue in the ovaries which exists as a small solid mass or as a cystic lutein body. Careful inspection will frequently reveal the presence of more than one lutein body in the ovaries. As the condition is more common about the time of the menopause, the treatment consists of a thorough curettage for purposes of diagnosis, followed by destruction or removal of the abnormal ovarian tissue.

Summary

It appears then, that uterine bleeding can be accounted for by changes in the histology of the endometrium, and that variations from the normal here can be directly attributed to abnormal ovarian function. The cause, in turn, may be due to disease in the ovary itself, to disturbances in the function of the anterior pituitary or to inadequate nutrition.

Treatment

The methods to be adopted in the treatment of menstrual abnormalities depend entirely upon the diagnosis of the cause, and are therefore individual in application. Treatment can be divided into four classes:

(1) Conservative with attention to measures which promote general health.
(2) Hormone therapy.
(3) Surgery.
(4) X-ray or Radium.

CONSERVATIVE TREATMENT

In the absence of malignancy and retained products of a pregnancy, irregular or prolonged menstrual bleeding are symptoms which frequently clear up without any treatment. This is particularly true of these symptoms when they result from a mild tubo-ovarian infection of the influenzal type. More virulent infections of the tubes and ovaries such as those in which the gonococcus is the active germ, require prolonged rest with the application of heat.

There is a very definite place for prophylactic treatment in regard to the direct and embolic infections in the female reproductive tract. Rest in bed should be compulsory for all women between the age of puberty and the menopause, during the time when they show an elevation of temperature from any generalized infection. The modern girl has to be protected from herself in still another way. The evils of inadequate food intake in order to keep slim are evidenced in the reproductive mechanism very early. These cases are amongst the saddest that one sees in private practice. The body needs an adequate supply of proteins and fats for

the normal action of the reproductive system.

HORMONE THERAPY

By means of substitutional ovarian hormone therapy, that is, the intramuscular injection of potent preparations of oestrin and progestin, the various activities of the uterine musculature and the changes in endometrial tissues can be absolutely controlled in uteri which are free from disease. It is obvious that the use of these substances in the treatment of menorrhagia or metrorrhagia that is primarily caused by altered ovarian function, can only be of temporary value. Attempts to control the ovarian cycle by the administration of gonadotropic principles are still very much in the experimental stage. There are, however, numerous reports in the literature in which beneficial effects in the treatment of uterine bleeding have been claimed as a result of the administration of anterior-pituitary-like substances. So far as I am aware no one has as yet observed any distinct microscopic or macroscopic changes either in the diseased endometrium or in diseased ovaries with arrested follicular development from this form of treatment.

Our education in reproductive physiology has been distinctly improved since the discovery of these hormones. Clinicians have learned to observe cases suffering from irregular bleeding over a longer period of time while waiting to see the effects of hormone therapy. It is impossible to calculate the number of patients who have escaped from unnecessary operative interference as a result of this prolonged study of their condition.

TREATMENT BY SURGICAL OPERATIONS

Every gynaecologist who has a thorough knowledge of the biochemistry of the ovarian hormones, and the variety of the effects of these substances on the reproductive system and on the social and the economic existence of the human female, realizes that the unnecessary removal of healthy ovarian tissue in the treatment of uterine bleeding during the reproductive period, is an act which should be listed in the criminal code. There are few diseases in the reproductive tract apart from malignant states and extensive ectopic endometrial implantation that call for the removal of healthy ovarian tissue in the treatment of uterine bleeding in patients up to the age of forty. Surgical removal of diseased ovarian tissue in young women, and the removal of diseased or healthy ovarian tissue for good reasons after patients have reached their late thirties, has to be considered in respect of the indications for such an operation in each individual case.

X-RAY OR RADIUM

Treatment of uterine bleeding by the use of X-ray or radium should only be undertaken as a last resort, except in cases where the bleeding is the result of a malignant growth in the reproductive tract. This method is of greatest value in the treatment of severe uterine haemorrhage from a prolonged oestrin or progestin phase in the endometrium during the menopause when the remaining ovarian tissue can be sacrificed.

CONCLUSION

In conclusion, may I hope that I have enlisted the faculties of the reader in a most interesting study—a study which it is impossible to elucidate in one brief paper. One should remember that up until the time of the isolation of the oestrogenic substances, no one had succeeded in isolating a single substance from the body fluids of the human which would cause such a rapid division and growth in epithelial cells as is effected by the ovarian hormone. This achievement was responsible for opening up new lines of approach to the solution of problems in gynaecology, including the cause of uterine bleeding. In addition one has only to add

the abnormal chronic irritation which is present at most cancerous sites in the endometrium to the continuous urge to divide which is supplied by oestrogenic substances, and you have the basic cause of the unbridled unnatural division of the invading cells which characterize cancerous growths in the reproductive tract.

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INTRACRANIAL ANEURYSMS

By J. CLIFFORD RICHARDSON, M.D., M.R.C.P., (Lond.)

Aneurysms of cerebral arteries occur almost exclusively in and around the circle of Willis. They are of considerable importance because of their fairly common occurrence, and because of their tendency to rupture producing haemorrhage into the subarachnoid space. Such aneurysms are found in from 1 to 1½% of routine autopsies. Spontaneous subarachnoid haemorrhage, which is one of the commonest forms of intracranial haemorrhage, is almost always caused by an aneurysm.

Pathology

MACROSCOPIC FEATURES

Basal cerebral aneurysms are of a rounded saccular type and tend to occur in the angles formed by the bifurcation or branching of the arteries. They are most commonly of a small size, averaging from 3 to 10 mm. in diameter. From their appearance they have been very suitably named "berry" aneurysms. (The term "berry" aneurysm will be used synonymously with "Congenital" and "saccular" aneurysm in this paper.) Occasionally they grow to a larger size and may measure 1 or 2 inches in diameter. Most often a single aneurysm is present, but two, three or four aneurysms are not uncommonly found in the same case. In the Department of Pathology of this University, 27 cases, with 40 aneurysms were encountered in routine autopsies over a period of 7½ years.

The aneurysms occur with equal frequency in the vertebral and carotid arterial systems. The commonest site is on the middle cerebral artery, either at its point of junction with the internal carotid, or at the origin of one of its main branches. The other large arteries are involved only slightly less often. Different statistical studies show that the arteries are affected in approximately the following frequency:—middle cerebral, internal carotid, basilar, anterior communicating, anterior cerebral, posterior cerebral, vertebral and posterior communicating, respectively. In a case with one or more berry aneurysms, the arteries at the base of the brain often look otherwise perfectly healthy; there may be coincidental arteriosclerotic changes or anomalies of distribution.

MICROSCOPIC EXAMINATION

The wall of a typical small saccular aneurysm is composed chiefly of thinned out fibrous connective tissue from the media of the artery. Muscle and elastic tissue usually disappear in the neck of the aneurysm and are not seen in the wall of the sac. There is usually a thick hyalinized atheromatous intima. Macrophages and polymorphonuclear leucocytes filled with yellowish blood pigment are often seen in the inner part of the wall. Heavy deposits of calcium sometimes appear in the deeper layers of the intima. The cavity of the aneurysm may contain fluid

blood, but on the other hand is often completely filled by old laminated thrombus.

PATHOLOGICAL FINDINGS AFTER HAEMORRHAGE

The haemorrhage from a ruptured aneurysm may extend into one or more of several different regions, subarachnoid, subdural, intracerebral, intraventricular, or into the cavernous sinus. In the vast majority of cases the rupture occurs directly into the subarachnoid space.

In a case of fatal haemorrhage, the whole base of the brain is covered by a thick layer of blood clot, filling the basal subarachnoid cisterns, and spreading out in a variable extent, to the outer and upper surfaces of the cerebral and cerebellar hemispheres. The origin of the haemorrhage is at first obscured by the blood clot. With careful dissection a berry aneurysm with a ragged tear in its wall, is found in the interpeduncular cistern, in the stem of the longitudinal or one lateral fissure, or on one side of the brain stem. The aneurysm may lie imbedded in cerebral tissue of a temporal or frontal lobe. In such cases blood may erode into the cerebral tissue and lateral ventricles, as well as into the subarachnoid space. The outer surfaces of the cerebral convolutions are flattened by increased intracranial pressure.

Signs of old haemorrhage may be in evidence, as areas of brownish staining by blood pigment, and thickening and adhesions of the leptomeninges.

NEIGHBOURHOOD LESIONS

A large aneurysm may compress and erode its surrounding structures, including cranial nerves, bony structures, cerebral cortex, and the brain stem. A small aneurysm likewise may damage surrounding soft tissues, particularly cranial nerves, directly by haemorrhage and by adhesions due to old haemorrhage. These focal lesions are of considerable clinical significance, and will be mentioned later in that regard.

Aetiology

The usual age incidence of cerebral aneurysms, from autopsy studies, may be roughly stated as from 15 to 60 years. Only occasionally are they found in younger children. The average age of meningeal haemorrhage due to aneurysm is a little younger, with an average of about 35 years. The sexes are equally affected.

There are three aetiological types, "Congenital," "Arteriosclerotic," and "Mycotic" aneurysms. Syphilis, the cause of more than 90% of aneurysms elsewhere in the body, plays a negligible role in causing intracranial aneurysms. The arteries here concerned are small muscular arteries, in which type of vessel syphilis causes endarteritis and thickening, rather than weakening and dilatation. Very rarely syphilitic aneurysms of the basilar artery have been found.

Aneurysmal dilatation may occur as a result of severe cerebral arteriosclerosis, but this is relatively uncommon. Such arteriosclerotic aneurysms involve chiefly the basilar and internal carotid arteries. They are fusiform dilatations of the trunk of the vessel, rather than the usual saccular outbranchings at points of bifurcation. When the latter, berry aneurysms, occur in association with cerebral arteriosclerosis, it is difficult to say whether the relation is aetiological or merely coincidental. Some workers believe local arteriosclerotic changes to be the cause of the usual type of saccular aneurysms.

Mycotic aneurysms are rare, and occur as a result of septic emboli, particularly in subacute bacterial endocarditis. The embolus nearly always lodges in either middle cerebral artery, causing a local infection and weakening of the wall and producing a saccular aneurysm of the artery in the Sylvian fissure.

The common berry aneurysms which have been above described, are not apparently due to either septic emboli or arteriosclerosis. They are generally

spoken of as congenital aneurysms and there is considerable evidence that they are developmental in origin. Their position in the angles formed by bifurcation of arteries suggests some local weakness peculiar to those points. Several years ago Eppinger, and later Fearnsides suggested that there were congenital defects in the structure of the cerebral arteries at the angles of bifurcation. More recently Forbus demonstrated a local absence of muscle of the medial coat at these points, and suggested that these are areas of congenitally defective structure of the arteries, which subsequently become dilated to form saccular aneurysms. Much less commonly aneurysms of the same type are found elsewhere in the body, particularly in abdominal arteries. Recently Nevin and Williams reported a case in which a fatal haemorrhage resulted from an aneurysm of the splenic artery, and multiple berry aneurysms were found on the cerebral arteries. Occasionally cerebral aneurysms have been found in association with congenital stenosis of the aorta. In such an event there are two possible factors, associated congenital lesions, and also the increased pressure in the carotid arterial system. These observations, then, all point strongly towards a congenital or developmental cause. No other satisfactory explanation has been offered for cerebral aneurysms. Further studies of these defects at the bifurcation of cerebral arteries are needed before this theory can be considered as fully proven.

Clinical Manifestations

The usual fate of a "congenital" berry aneurysm is to rupture producing the clinical picture of spontaneous subarachnoid haemorrhage. Such haemorrhages may be small, with recovery. Complete recovery is possible but there are frequently recurrences and finally a larger fatal haemorrhage. On the other hand, there may be no symptoms prior to a sudden rapidly fatal large haemorrhage. Occasionally an aneurysm does not rupture but becomes sufficiently large to press upon neighbouring structures giving rise to focal symptoms in the same way as does a tumour at the base of the brain. A considerable number of the aneurysms remain small and silent, producing no symptoms during life, and being found accidentally at post-mortem.

The symptoms thus depend upon the nature of the wall of the sac, and the size and position of the aneurysm. They may be classified as follows:— 1. Spontaneous Subarachnoid Haemorrhage, occurring with no previous symptoms. The symptoms and prognosis will vary with the size of the haemorrhage. 2. Spontaneous Subarachnoid Haemorrhage, with preceding localizing symptoms due to neighbourhood lesions. 3 Local Symptoms only, due to an unruptured large aneurysm producing pressure symptoms as a tumour does. In some of such cases there may be a history of previous small haemorrhages.

Some of the symptoms of aneurysm will now be considered in more detail.

SPONTANEOUS SUBARACHNOID HAEMORRHAGE

The symptoms usually develop during some exertion or excitement, though they may appear while the patient is at rest. There is a strikingly sudden onset of severe headache, like being struck a heavy blow to the head. The pain is usually most severe in the occiput, but may be generalized, vertical or unilateral. With a large rupture of the aneurysm consciousness is soon lost, the patient lapses into a deep coma and dies within a few hours.

With a smaller haemorrhage unconsciousness is transient or may not occur. Accompanying the headache, vomiting and intense giddiness frequently occur. After the first hour or two, the patient is in a confused, irritable, drowsy state. Now the headache characteristically radiates down the back of the neck. The patient resents any movement of the head or limbs. Due to the pressure and irritation of the blood in the subarachnoid space, the clinical

signs of meningeal irritation, such as stiffness of the muscles of the back of the neck, and Kernig's sign, are present. A moderate elevation of temperature from 99 - 101° F. is common. Albuminuria and glycosuria are sometimes produced.

Ophthalmoscopic examination often yields particularly valuable information. A slight degree of papilloedema is generally present. Retinal haemorrhages are seen in most cases. These are usually small, and situated along the vessels near the disc. Larger, rapidly-developing subhyaloid haemorrhages sometimes occur, and are highly characteristic of this disease. The haemorrhages are not due to subarachnoid blood passing into the eye, but are probably due to compression of the central vein of the retina by blood under pressure in the optic nerve sheath. Papilloedema and ocular haemorrhages are probably more common when the aneurysm is in the anterior group of vessels.

The reflexes may be altered by the increased intracranial pressure. Thus all of the tendon jerks and the abdominal reflexes are frequently much diminished or absent. Bilateral extensor plantar responses, without gross loss of power in the legs, are likewise produced.

Examination of the cerebrospinal fluid by lumbar puncture provides the essential clue to the diagnosis of subarachnoid haemorrhage. The pressure is elevated in the early days. The fluid is deeply and evenly blood-stained. When allowed to stand the red blood cells settle out and there is no clotting. Within the first few hours after the onset, the supernatant fluid is clear, but after about 12 hours it is distinctly yellow. The red blood cells disappear in 3 or 4 days, the xanthochromia after 2 or 3 weeks.

As well as the above symptoms produced by subarachnoid blood and increased intracranial pressure, there may be others due to focal compression or erosion of brain tissue and cranial nerves by the haemorrhage. Invasion of cerebral cortex and white matter in different areas may cause convulsions, aphasia, hemiplegia or hemianopia. Gross lesions of the pyramidal tracts are not very common. Pressure or invasion of one optic nerve may produce partial or complete monocular blindness. The cranial nerves most frequently affected are the 3rd., 4th. and 6th., producing ocular weakness and a strabismus. The condition called ophthalmoplegic migraine is said to be produced by a berry aneurysm, probably as a result of repeated small haemorrhages in the region of oculomotor nerves. Occasionally severe root pains in the trunk and legs are produced by blood irritating spinal nerve roots.

Various clinical types of spontaneous subarachnoid haemorrhage which depend upon the severity of the bleeding, and its local effects, have been recognized, namely—comatose, meningitic, convulsive, psychotic, ophthalmoplegic, hemiplegic, migrainous and lumbago-sciatic types.

The main essential of treatment is complete rest for several weeks to enable the ruptured aneurysm to become thrombosed and healed, and to prevent a second haemorrhage. Repeated judicious withdrawal of bloody cerebrospinal fluid is carried out with the object of reducing the intracranial pressure to normal and minimizing sequelae by removal of the irritating blood.

Recovery from the acute attack occurs in about 50% of cases as shown by the reviews of Hyland, (C.M.A.J. 1933), and others. Recovery may be complete but there are often residual symptoms indicative of permanent damage. Headaches are frequent. There may be mild or severe intellectual impairment. A squint and diplopia due to oculomotor paralysis is common. A hemiplegia may persist; this is one of the commonest causes of hemiplegia of vascular origin in a young adult. Visual impairment due to haemorrhages in the eyes and visual pathways, may remain. Epileptic convulsions sometimes continue to occur after a haemorrhage. There is a definite tendency to recurrence of

spontaneous subarachnoid haemorrhage.

LOCAL PRESSURE SYMPTOMS

When an aneurysm does not bleed, but becomes sufficiently large to press on surrounding structures, its symptoms are those of a tumour in the same position. Aneurysms of the anterior group of vessels, (middle and anterior cerebral, internal carotid and anterior communicating), affect chiefly the optic, oculomotor and trigeminal nerves. Thus may be produced a nasal field defect by pressure on the outer side of one optic nerve, a squint and diplopia by pressure on the third, fourth or sixth nerves, and pain and impaired sensation on one side of the face, particularly in the distribution of the ophthalmic division of the fifth nerve. There have rarely been cases with symptoms of hypopituitarism due to compression of the pituitary gland by an aneurysm in that region. Aneurysms of the vertebral and basilar arteries produce localizing pressure symptoms more often, because they tend to become larger, and because they have less room to expand around the brainstem. A third or seventh nerve paralysis, with a "crossed," contralateral hemiplegia due to pressure on the adjoining pyramidal fibres in the midbrain or pons, may be produced. The clinical picture is occasionally that of a tumour in the cerebello-pontine angle, with lesions in some or all of the lower six cranial nerves, cerebellar signs and hydrocephalus due to compression of the aqueduct.

X-RAY FINDINGS

Abnormalities which can be recognized in x-ray films are occasionally produced by calcification in the wall of the sac and by erosion of adjacent bony structures. Calcification, when present, is very characteristic and appears as a sharp thin curved streak, known as an Albl's ring. Erosion of one or both clinoid processes on one side, or of the sphenoid, or of the margins of the superior orbital fissure, have been described. Aneurysms have also been demonstrated radiologically, by the injection of thorotrast, a radio opaque substance, into the internal carotid artery. This method is not infallible because sometimes the aneurysmal sac is filled with thrombus so that thorotrast cannot enter it. There are certain difficulties and dangers of such thorotrast injections, so that it is not now very extensively used.

THE DIAGNOSIS OF INTRACRANIAL ANEURYSMS

The clinical diagnosis of berry aneurysms is now more frequently and correctly made than in the past, because of increased knowledge and interest in recent years.

In the common clinical group in which an attack of spontaneous subarachnoid haemorrhage occurs without any previous symptoms, the diagnosis, though presumptive, is strongly in favour of aneurysm. A history of repeated attacks is pathognomonic.

When local pressure symptoms suggesting a tumour at the base of the brain, is the entire clinical picture, the diagnosis of aneurysm is impossible unless there should be sufficient calcification to show the characteristic x-ray shadow. The diagnosis will be more often made when the possibility of aneurysm is kept in mind in cases where there are symptoms of a basal cerebral tumour.

If there is a history of repeated attacks of subarachnoid haemorrhage as well as local pressure symptoms, the diagnosis of aneurysm is almost certain.

The full differential diagnosis of berry aneurysms will not here be considered. From previous remarks, some of the diseases from which it must be differentiated are obvious—intracerebral haemorrhage, meningitis, encephalitis and cerebral tumours.

The possibility of surgical treatment by ligating arteries or resecting aneurysms, remains undecided but seems to offer very little hope of cure.

Less Common Types of Intracranial Aneurysms

Arteriovenous aneurysm of the internal carotid artery is quite a different condition from the usual berry aneurysm. As a result of a head injury with a fracture of the cranial base, a tear in the internal carotid artery in the cavernous sinus, is produced. Consequently there is a free arteriovenous communication between the artery and the venous blood of the cavernous sinus. Marked distension of the sinus and its tributaries may be produced. The clinical picture is characteristic. There is a loud systolic bruit in the head which can be heard by auscultating the skull, and is usually heard very distressingly by the patient. The eyeball on the side of the aneurysm pulsates and is pushed forward — a pulsating exophthalmos. The veins of the eyelids, conjunctiva and retina are congested and there is usually a partial or complete ophthalmoplegia. Bruit in the head—cephalic bruit, has not been mentioned above amongst the symptoms of berry aneurysm. It is stated to be found very occasionally with large saccular aneurysms, but its actual incidence is so very rare as to warrant disregarding it. Cephalic bruit is produced by traumatic arteriovenous intracranial aneurysm, by arterial angioma of the brain and occasionally by a vascular meningeal tumour. A faint bruit may be heard normally in infants.

Miliary intracerebral aneurysms were described many years ago by Charcot and Bouchard as the cause of the common intracerebral haemorrhages in the region of the internal capsule. Various observers since have failed to find true aneurysms of the small intracerebral arteries and suggest that what Charcot described were only minute dissecting aneurysms in severely arteriosclerotic arteries.

Arteriosclerotic and mycotic aneurysms have been mentioned above in the discussion of aetiology. These types of aneurysms may present the same clinical features as congenital berry aneurysms, with the addition of the symptoms of the causative disease, namely cerebral arteriosclerosis and subacute bacterial endocarditis. Cerebral arteriosclerosis may manifest itself in an elderly person or a middle-aged hypertensive by memory defects, slowing of thought processes, emotional disturbances, signs of focal cerebral softening, and signs of advanced peripheral and retinal arteriosclerosis. If such a patient develops the symptoms of subarachnoid haemorrhage or pressure on cranial nerves, the diagnosis of an arteriosclerotic cerebral aneurysm is very likely. The symptoms of a mycotic cerebral aneurysm are usually over-shadowed by those of the underlying septic endocarditis. The picture may be that of a sudden hemiplegia of embolic origin, followed several weeks later by spontaneous subarachnoid haemorrhage from rupture of a mycotic aneurysm.

Subjoined is an abbreviated report of a case with two typical berry aneurysms, one of which had ruptured producing a fatal haemorrhage.

The patient, a man of 41 years of age,

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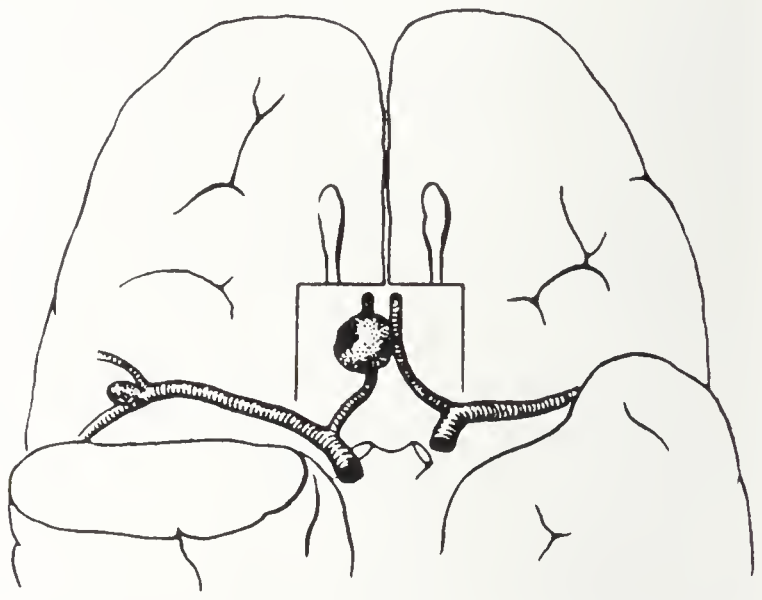
was well until a few hours before death. He suddenly suffered severe pain in the head, particularly over the right eye. He became mentally confused and excited and later lost consciousness, dying within three or four hours of the onset of symptoms. No medical examination was made before death.

Post-mortem examination of the brain showed marked subarachnoid haemorrhage at the base, filling the cerebello-medullary, pontine and interpeduncular subarachnoid cisterns. Dissection showed a round saccular aneurysm, 1 cm. in diameter, arising from the anterior communicating artery. The aneurysm extended forwards between the two anterior cerebral arteries, and had thickened opaque areas of atheroma in its wall. A small rupture was present in its right upper surface and the haemorrhage had eroded through the floor of the anterior horn of the right lateral ventricle. Sections of the brain showed blood in all the ventricles. A small unruptured aneurysm was present on the right middle cerebral artery in the Sylvian fissure. This aneurysm was oval and saccular, about 4 mm. in length, and attached to the apex of the angle between the right middle cerebral artery and its first branch. (Specimen No. 2478. Pathological Museum). This case is reported with the kind permission of Prof. E. A. Linell.



A drawing showing the ruptured aneurysm of the anterior communicating artery and the small intact aneurysm of the right middle cerebral artery. The blood clot has been removed and portions of the frontal and right temporal lobes resected. The anterior communicating artery is hidden by the larger aneurysm.

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ACUTE INTESTINAL OBSTRUCTION

By DANIEL LEVY, '38.

Acute intestinal obstruction is the condition in which passage of contents along the intestinal canal is more or less suddenly obstructed either completely or in greater part. The obstruction may be primarily acute or else secondary to a chronic obstruction, and it is one of the three basic conditions in the peritoneal cavity which constitute abdominal surgical emergencies, the other two being acute inflammation and haemorrhage. In large hospitals, the mortality figures from acute intestinal obstruction run from 40-50% and even higher and so we see the importance of this condition and the necessity for making a correct diagnosis early and applying proper therapeutic measures at once.

Aetiology and Classification.

Acute intestinal obstruction causes may be divided into two broad groups: (a) Mechanical obstruction; (b) Obstruction due to nervous imbalance. These two groups may be subdivided further, as follows:

A. MECHANICAL OBSTRUCTION.

1. *Causes within the lumen of the bowel.*

(a) *Gall stones*—enter the bowel through a cholecysto-duodenal or other fistula and lodge usually in the lower ileum.

(b) *Faecal accumulations*—are commonly the cause of acute following chronic obstruction.

(c) *True foreign bodies*—very rarely.

2. *Causes in the wall of the bowel.*

(a) *Neoplasms*—carcinoma is the commonest. One usually finds a chronic obstruction and then an acute termination due to an impaction of faeces, twisting of a distended coil or an acute paralysis of the intestinal wall.

(b) *Congenital stricture*—is a rare cause in early infancy, the stricture being found either at the rectum, in the duodenum just proximal to the entrance of the bile ducts or at the site of a Meckel's diverticulum.

(c) *Acquired stricture*—due to a stenosing type of carcinoma, diverticulitis or a traumatic stricture, e.g. following suture of bowel.

3. *Causes outside the bowel*—are the ones most frequently seen.

(a) *Obstruction due to herniation.* This may be either external or internal herniation and is often associated with strangulation of the involved loop of bowel. Of the external herniation group the most common is the femoral type, followed by inguinal, umbilical and incisional types. Internal herniation may occur either through congenital or acquired slits or tears in the mesentery or omentum, through one of the normal peritoneal fossae, e.g., at the duodeno-jejunal flexure, in the peri-caecal region or in the root of the pelvic mescolon, or more rarely, through the foramen of Winslow or through congenital or acquired apertures in the diaphragm.

(b) *Obstruction and strangulation due to bands and adhesions.* These may be either congenital, inflammatory, from adherence of normal structures or resulting from a persistent Meckel's diverticulum. In the latter case, obstruction is caused either by bridging across a portion of bowel, by twisting about a knuckle of bowel or by causing a kinking of the bowel.

(c) *Compression from without by tumor, enlarged lymph glands, etc.* This type of obstruction occurs especially where the gastro-intestinal tract is fixed, e.g., at the retroperitoneal duodenum, at the terminal ileum and in the pelvis.

4. *Intussusception*—a telescoping of one segment of bowel into another immediately below it.

5. *Volvulus*—a torsion or twisting of a coil of bowel on itself around its mesenteric axis.

B. OBSTRUCTION DUE TO NERVOUS IMBALANCE.

1. *Paralytic Ileus*—a paralysis of the muscular walls of the bowel following an abdominal shock, e.g., after abdominal operations or injuries, after peritonitis, also associated with pneumonia, pleurisy, fractures, heart disease, etc.

2. *Spastic Obstruction*—seen when spasm of bowel occurs, usually along with an intraluminal irritant, e.g., gall stones, parasites.

3. *Vascular Occlusion*—really a paralytic ileus.

a. Mesenteric embolism—seen in heart disease.
b. Mesenteric thrombosis—seen in septic abdominal conditions and in cirrhosis of the liver.

In order of frequency, one finds that strangulation from external herniation causes 30-40% of all acute obstructions, followed closely by bands and adhesions, next by intussusceptions which cause over 75% of all obstructions in children under two years, and then by neoplasms which cause about 18% of all intestinal obstructions. Of the neoplasms, it is interesting to note that carcinoma of the rectum and sigmoid cause about 85% of all acute obstructions in the colon.

Pathology.

In the majority of cases of acute obstruction there is, in addition to obstruction of the lumen, strangulation of part of the bowel, which implies a constriction of and impediment to its blood supply. Thus we shall consider the pathology of acute intestinal obstruction in three regions; above the obstruction, below the obstruction, and in the strangulated coil itself.

Intestine above the Obstruction.—This part of the bowel is greatly distended by gas and fluid, the latter consisting of the normal secretions to which is added an exudation of serum. The walls are at first pale and thin but as the obstruction continues, they become purple and thickened with oedema, and the mucosa becomes eroded and stercoral ulceration results. Finally the bowel becomes paralysed and bacteria are allowed to escape into the peritoneal cavity through the distended coils to give rise to peritonitis. As a result of the peritonitis other parts of the bowel may become involved in a paralytic ileus.

Bowel below the Obstruction.—Here one usually finds the coils empty, contracted and pale as a result of the reflex violent peristalsis set up at the time of the initial obstruction and strangulation.

Bowel of the Strangulated Loop.—Because of the pressure on the veins at the point of strangulation, the wall of the bowel becomes purple, thickened and oedematous by engorgement of the blood vessels and an exudation of serum and white blood cells. Capillary haemorrhages are common and a fibrinous exudate covers the peritoneal coat of the bowel. With further swelling and oedema, the arteries also become obstructed and then the loop rapidly becomes gangrenous, allowing the escape of bacteria into the peritoneum, or else actual perforation occurs through the distended and weakened walls.

Biochemical Upsets in Acute Obstruction.

In acute intestinal obstruction, with its accompanying loss of fluids in the vomitus and the drainage of large quantities of fluid into the distended bowel proximal to the obstruction, there occurs, in addition to the intense *dehydration*, characteristic changes in the blood chemistry. (a) *There is a decrease in blood chlorides* (as a result of the loss of free hydrochloric acid in the vomitus or into the lumen of the intestine and not reabsorbed). (b) There is an *increase in the CO_2 combining power*, i.e., an increase in the alkali reserve (due to the attempt of the bicarbonate ions to replace the lost chlorine ions).

(c) There is a *rise in the N.P.N. content of the blood* (due to the increased destruction of protein and the decreased circulation volume and urine output as well as toxic damage to the kidneys).

These blood changes described occur especially in high intestinal obstruction. When obstruction occurs in the lower ileum or in the colon, the electrolytes, whch are seriously depleted in high obstruction, are afforded an opportunity for at least partial reabsorption, and so the symptoms are much less severe. Thus, in high obstruction, the administration of saline solution appears to act almost like a specific since it adequately substitutes for the fluids and electrolytes lost.

What Causes the Symptoms and Death in Acute Obstruction?

Several theories have been put forward to explain the symptoms and death in acute obstruction. A brief summary of the more important ones will be outlined.

TOXIC THEORY.

(a) *Bacterial toxins* as a result of growth of bacteria, especially B. welchii, in the obstructed bowel give rise to a toxemia.

(b) Toxins, especially *histamine,* from the bacterial decomposition of *proteins* in the lumen of bowel above the obstruction (Gerard).

These theories are disproven on the grounds that all the symptoms are less acute and life more prolonged, when the obstruction is low down, whereas in this region the bacterial growth, protein decomposition and histamine concentration are at a maximum.

(c) *Proteose* from the mucosa of the obstructed bowel. (Whipple and his associates). Extracts of mucosa from obstructed bowel injected intravenously in normal animals caused symptoms very similar to intestinal obstruction. Thus Whipple claims that death is due to a toxemia from absorption of the toxic proteose formed in the mucosa of the obstructed bowel. This has not been confirmed by other investigators as yet.

DECHLORINATION AND DEHYDRATION THEORY.

Numerous observers have attempted to explain the symptoms and death in intestinal obstruction on the basis of the profound biochemical upsets which occur, stressing especially the loss of chlorides. However, it has been shown that normal animals, who have had the chloride content of their blood greatly reduced by injections of histamine (which stimulates secretion of gastric juices) and apomorphine (which causes vomiting) remained in apparent good health even though their blood chlorides were maintained at a level of 50% of normal for three weeks. Nevertheless, it seems probable that dechlorination and dehydration do play an important part in the later stages of obstruction since the administration of saline acts so dramatically.

THEORY OF NERVOUS MECHANISM.

Taylor, Weld and Harrison, in a series of brilliant experiments, have shown the possibility of a nervous reflex element as the causative factor in the symptoms of intestinal obstruction. Using a balloon to which was attached a large sized rubber tube, they passed it into the lower duodenum and inflated the balloon. In this way the bowel wall was distended and at the same time bowel contents were allowed to pass along the lumen through the rubber tube. When the balloon was pumped up to 100 mm. mercury, the animal showed the same symptoms as seen in acute obstruction and yet neither dehydration nor dechlorination were present. It is possible that distension of the bowel set up nervous impulses which reflexly affected the cardio-vascular, digestive and other systems, giving rise to the symptoms and signs of acute intestinal obstruction.

SHOCK.

Moon and Morgan give autopsy evidence to show that death following intestinal obstruction results from circulatory failure of the shock type. The gross and microscopic visceral changes

in death from obstruction were identical with those changes that accompany shock produced by other means. They suggest that the probable cause of the shock syndrome is intoxication either by histamine, bacterial toxins or products of injured tissue.

Signs and Symptoms.

It is of the greatest importance for one to get a clear, accurate picture of the signs and symptoms of *early* acute intestinal obstruction since it is only by correct diagnosis of the condition in this stage that life-saving measures may be applied with good results and the appalling mortality rate reduced.

The usual text-book description of acute intestinal obstruction, which describes the patient as acutely ill, shocked, with pale and pinched facies, rapid, thready pulse, subnormal temperature and cold, clammy extremities, gives one an end-stage picture of the condition, and has been the cause for many late diagnoses of obstruction. As Dr. R. R. Graham has stated, *in early acute obstruction the patient does not look ill or shocked and his pulse and temperature are normal. He complains of rhythmical colicky pains and is nauseated, the pain and nausea continuing in spite of sedatives.* It should be remembered that simple acute obstruction is the only serious acute abdominal condition which does not cause abdominal tenderness, but one must not consider the lesion trivial because of this lack of tenderness.

The classical symptoms of acute intestional obstruction are *pain*, *vomiting* and *constipation*. (a) *The pain* is intermittent and colicky and represents an overactive persistalsis attempting to overcome an obstruction. It comes on early, often sudden and is severe, rising to a peak which it maintains for one or two minutes and then stops abruptly only to return after a short interval of comfort. (b) *Vomiting* may occur at the onset of the acute obstruction through a reflex mechanism. Very early in the obstruction only nausea is present but later with complete high small bowel occlusion, accompanied by a damming back of gastric and other digestive juices the vomiting is frequent and copious. In low obstruction, especially in the left colon, no vomiting at all may occur although great distension is present. When the vomitus becomes stercoraceous, the condition is very late and is invariably fatal. (c) *Constipation,* after the first few hours, is absolute for both faeces and flatus. At the onset, the bowel distal to the obstruction may empty itself, or an enema may appear effectual since it washes out this distal part of the bowel. A bowel movement that gives relief indicates that obstruction is not complete. Later in complete obstruction, the patient often feels the desire, but is unable to pass flatus.

The earliest, most constant and, therefore, most important sign of acute intestinal obstruction is auscultatory evidence of hyperperistalsis and intestinal colic. On auscultation, gurglings, heard best at the height of a colicky intermittent pain, establish definitely that a mechanical block is present. Inspection of the abdomen may reveal visible peristalsis, indicating that the acute obstruction has complicated a chronic obstruction. Visible peristalsis means hypertrophy of the muscular coat and this hypertrophy requires at least one week before visible evidence occurs. Of course, in very thin subjects visible peristalsis may be normally present, whereas in fat individuals with obstruction, visible peristalsis may never be seen. Distension and increased tympany are present later in obstruction, especially when the block is low in the bowel, although it occurs early in volvulus. Rectal examination must never be omitted, as it may reveal the cause of the symptoms, e.g., neoplasm, faecal impaction.

SPECIAL EXAMINATIONS.

1. *X-ray* is very valuable in establishing or confirming a diagnosis of intestinal obstruction. In adults and children over three years of age, gas in the alimentary canal, excluding the stomach and colon, is not visible in X-ray because it is so closely mixed with the fluid. How-

ever, in obstruction, the gas separates and in an X-ray picture taken with the patient erect, *fluid levels* are seen and indicate intestinal stasis.

Two characteristic arrangements of gas in the small intestine have been observed in X-ray; (a) a *feathery, herring-bone appearance* due to prominence of the plicae circulares and is very suggestive of obstruction; (b) the pathognomonic *step-ladder like arrangement* of the parallel loops of gut. DeCourcy states that this latter appearance comes late and may not be present in the first X-ray taken and so one should not wait for it in arriving at a diagnosis. X-ray following a barium enema is valuable in locating the site of obstruction.

2. *Blood*: In early obstruction, blood findings are normal. Later, with dehydration and consequent concentration of the blood, increased values for haemoglobin, red and white blood counts will be obtained. Blood chemistry findings, as stated previously, are decreased blood chlorides, increased CO_2 combining power and elevated N.P.N. but these are seen only after 48 hours and especially in high intestinal obstruction. They are of no definite diagnostic value except in atypical cases, but are useful in following the recovery of a patient.

3. *Urine* is scanty and may show some albumin or casts. Proper treatment with saline intravenously soon corrects the anuria and the abnormal findings disappear.

Diagnosis

It is essential, once intestinal obstruction is established, to determine the type and site of the obstruction. A careful history, an examination of hernial rings, rectum, post-operative scars, and investigation of any findings suggestive of malignancy, will establish the cause of obstruction in 75% of the cases. Other findings on physical examination which are suggestive are; signs of congenital anomalies, e.g. polydactylism, would make one suspect Meckel's diverticulum; visceroptosis suggests volvulus; heart disease with embolic phenomena suggests mesenteric artery occlusion; cirrhosis of liver or a septic abdominal process suggests mesenteric vein thrombosis; venereal disease, tuberculosis, perineal lacerations during delivery, all suggest stricture; a history of previous common duct obstruction would make one think of the possibility of a gall stone causing the obstruction; any previous acute inflammatory conditions e.g. salpingitis, appendicitis or cholecystitis suggests obstruction from adhesions and its site. In every case, high intestinal obstruction is much more severe and much more rapidly fatal than low intestinal obstruction.

When strangulation is present the condition is always more severe and demands prompt reduction before extensive necrosis and peritonitis occurs. The pulse is rapid, respirations are hurried and abdominal tenderness occurs early.

Paralytic ileus must be carefully differentiated from a mechanical obstruction because in the latter the treatment is immediate operation, whereas in paralytic ileus the treatment is medical. The diagnosis of paralytic ileus is made on the history and appearance of progressive distention of the abdomen usually following an operation, and the silent abdomen—no pain, no tenderness or rigidity, associated with effortless vomiting. This is in direct contrast to the colicky pains and auscultatory evidence of block in mechanical obstruction.

Volvulus, due to a twist of a loop of bowel in its long axis, occurs because of an abnormally long loop with a narrow mesenteric pedicle. Sigmoid volvulus accounts for 50% of these cases, followed by the caecum and terminal ileum. It is diagnosed by its sudden severe onset, usually during exertion, its location, and by the extreme abdominal distention that occurs early.

Intussusception occurs chiefly in male children in the fourth to the ninth month of life. 75% of the cases are in children under two years and can easily be diagnosed by its sudden onset in a child of robust health, periodic

attacks of pain, vomiting at onset, passage of mucus and blood per rectum, palpation of a sausage shaped tumor (60% of cases), and rectal examination in which the head of intussusception is felt or blood and mucus seen on examining finger.

There are certain factors which lead to delay in the early diagnosis of acute intestinal obstruction. The lack of local physical signs, e.g. no abdominal tenderness, may lead to the impression that nothing serious is impending. Again, enemas may give a return of gas and faeces and lead one to believe that no obstruction is present. The effectiveness of the enemas was due, however, to the presence of faeces below the obstruction. Another very important factor is the administration of morphine before a definite diagnosis has been made. Morphine will abolish intestinal colic and increase the tone of the bowel and thus cloud the symptoms and falsify the clinical picture.

Differential Diagnosis

The diagnosis may be difficult since stimulation of the abdominal sympathetic from whatever cause, produces similar symptoms. For example *appendicitis, renal calculus, biliary calculus, movable kidney* (Dietl's crisis), *twisted ovarian tumor* or *torsion of testes* will cause sympathetic stimulation and result in pain and vomiting. However, a careful history e.g. of chronic gall bladder disease, location and radiation of pain, and a careful physical examination e.g. palpable kidney or pelvic tumor, absence of one testes, will help to differentiate these conditions.

Acute haemorrhagic pancreatitis is difficult and practically impossible to differentiate. The diagnosis is suggested by the very rapid collapse, feeble pulse, usually distention high in the abdomen and a constipation which is not absolute.

Peritonitis from an appendicitis or ruptured peptic ulcer will be distinguished by the history and examination revealing a rigid, tender abdomen, pyrexia and vomiting small in amount. Any acute gastro-intestinal irritant giving an *acute enteritis* with crampy pains may be differentiated by the diarrhoea as well as the history and nature of the constitutional symptoms.

There is one condition that stimulates acute intestinal obstruction very markedly and that is *lead colic.* This condition may be differentiated by the occupational history, blue line on gums and by the simple injection of 5 cc. of 10% calcium chloride intravenously which abolishes the colic at once. Tabetic crisis is distinguished by the presence of other signs of tabes but one must remember that a syphilitic may get acute intestinal obstruction as well.

Prognosis

The mortality in acute intestinal obstruction has for many years been 40-50% and even higher, due chiefly to the delay in diagnosis and in the institution of adequate therapy. In strangulated hernia, where the diagnosis is obvious because the doctor can see the lump, treatment is quickly started and the mortality figures are low, 6-8%, showing that it is the delay in diagnosis that accounts for the high mortality.

The higher the obstruction, the more severe and more rapidly fatal is the condition. In a simple, non-strangulated obstruction of the colon, a patient may survive fairly comfortably for two weeks while waiting for operative relief.

Treatment

Once a diagnosis of acute mechanical obstruction has been made, the treatment is immediate operation to relieve the obstruction. The operation may be delayed for four or five hours in an attempt to restore the upset biochemical mechanism through administration of intravenous saline.

(1) *Pre-operative treatment*

(a) *5% glucose in normal saline intravenously*—1500-2000 c.c. This will counteract the dehydration and dechlorination and at the same time relieve the

starvation which may have resulted from the vomiting.

(b) *Continuous gastric suction tube* —to decompress the overdistended bowel. A large return of fluid and gas indicates a high grade of obstruction. With the intra-enteric pressure reduced, the colicky pains will be relieved, and as the distention disappears, palpation for tumor may be undertaken. In certain cases of mechanical obstruction due to adhesions, this treatment may overcome the obstruction, and as the oedema about the site decreases, the bowel again becomes patent.

(c) No morphine must be given until the diagnosis is made and the site of obstruction approximately located.

(2) *Operative treatment*

The purpose of the operation is to relieve the obstruction and no more. Never do a resection or an anastomosis of bowel at this stage. Some surgeons contend that if the patient's general condition seems good, resection of a growth may be done. This is a matter of the surgeon's judgment and experience, the safe procedure being to relieve the obstruction only.

Spinal anaesthesia should be used since the danger of aspiration of vomitus with a general anaesthetic is too great. Through a long abdominal incision, the caecum is palpated first and if it is full, the obstruction is in the large bowel, whereas if caecum is collapsed, obstruction is in the small bowel. In small bowel obstruction, collapsed loops are followed back to the site of the blockage and the cause verified. A constricting band may be divided, but if the obstruction is not easily relieved an enterostomy is performed proximal to the obstruction. A strangulation must be reduced and any gangrenous bowel must be pulled out through the skin incision and a proximal enterostomy performed. Resection of the devitalized bowel may be done later. In order to determine if the bowel is viable, one is influenced by its colour, the condition of the overlying peritoneum, presence of arterial pulsations in the mesentery, by bleeding when the peritoneum over the bowel is scraped and by careful observation of changes in the doubtful loop when covered with hot towels to see if the colour improves and peristaltic movements return.

In the large bowel, obstruction is due to carcinoma in 85-90% of the cases and the simplest and surest method of relief is to do a *caecostomy*. In two or three weeks, the growth, if considered operable, will be removed. Volvulus or strangulation from any cause must be relieved as in the small bowel.

(3) *Post-operative treatment*

(a) 5% glucose in normal saline intravenously—3000-5000 c.c. per day. Keep a chart of the fluid intake and output and gauge amount of fluid required.

(b) Duodenal tube to assure adequate decompression of bowel and also to control any vomiting.

(c) Nothing by mouth until all nausea and vomiting has stopped and peristalsis reestablished.

(d) To stimulate peristalsis, heat cradle to abdomen for one hour at least two or three times a day. Injections of pituitrin (1 c.c.) and eserine (gr. 1/50) q. 3. h. intramuscularly are also helpful.

Treatment of paralytic ileus is medical. Attempts are made to stimulate peristalsis by heat cradle or poultices to abdomen. Pituitrin and eserine as above should be injected. A duodenal tube is put in to relieve the distention and vomiting. Hypertonic saline (600 c.c. of 6% solution intravenously) has been suggested for stimulation of peristalsis. Many still give B. welchii serum (20 c.c. intramuscularly) to reduce formation of gas in the intestinal tract. High spinal anaesthetic has also been used but its effects are often transient.

Summary

Acute intestinal obstruction is a condition that demands early diagnosis and prompt treatment if the life of the patient is to be saved. The appalling mor-

tality figures of the past reflect upon the lateness of diagnosis in the majority of cases. This paper has attempted to outline the common causes of acute intestinal obstruction, the essential points for an early diagnosis and the therapy necessary to correct the profound chemical upset as well as to restore the patency and function of the bowel. Only with these facts in mind can we hope to appreciably lower the death rate from this condition and give the patient the best chance for recovery.

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A POSSIBLE RELATIONSHIP BETWEEN HYPERTHYROIDISM AND GALL BLADDER DISEASE

By D. L. CAMPBELL, '39.

AN INTERIM REPORT

This is an analysis of 60 cases of hyperthyroidism with the view of determining in how many of these cases there was previous gall bladder disease. The results are listed below.

Biliary Colic	3
Acute Cholecystitis	6
Cholecystic Indigestion	7
Cholecystectomy	5
Indefinite Epigastric distress	9
Negative	30
Total	60

Of these cases 4 were seen by the writer, 3 on the wards and one outside the hospital. These formed the basis for this analysis. 56 were taken at random from the files of case histories of patients operated upon in 1936 with the diagnosis of diffuse hyperplasia of the thyroid with hyperthyroidism. Of the 21 patients having previous gall bladder disease 18 were females and 3 males, 17 over 30 years of age and 4 under 30 years of age. Of the five patients who had previous cholecystectomy the intervals between operations were 3 months, 1 year, 8 years, 10 years, and 15 years. One interesting history was that of a woman aged 52. She had had cholecystic indigestion with two attacks of acute cholecystitis. Cholecystogram revealed a non-functioning gall bladder. Following her operation for relief of hyperthyroidism her gall bladder symptoms completely disappeared and she refused cholecystectomy.

8.4% of routine autopsies show gall stones. Of these 71.8% give rise to no symptoms.[1] Therefore about 2.4% of routine cases may be expected to have gall stones giving rise to symptoms. Going back to the figures above, well over 80% of all patients with inflammatory disease of the gall bladder have gall stones. 21 out of 60 cases reviewed had previous inflammatory disease of the gall bladder, that is 35%. Of these, 28% of the total 60 would have gall stones giving rise to symptoms. From these figures it would seem that gall stones are ten times more common in persons suffering from hyperthyroidism than in routine cases. However there is also the factor of age —the cases considered were divided according to age thus:

10-19	3
20-29	15
30-39	12
40-49	13
50-59	17

This appears to be an age distribution which could be compared with routine autopsy cases.

No attempt will be made here to compare fully these two diseases. The predisposing factors common to these two diseases are well known. A few of the more striking parallels are listed below.

Geographical incidence—Cholelithiasis is most common in the goitre regions of Canada, U.S.A., England, Germany, Switzerland, Austria and in India.[2]

Sex incidence—Various authors quote the incidence of these diseases to be in the ratio of 6 in females to one in males or 4 in females to 1 in males. In the short series above the ratio was 6-1..

Pregnancy—The thyroid becomes enlarged during pregnancy and lactation; gall bladder disease is 10 times more common in women who have borne children and often develops during or immediately after pregnancy.

Family predisposition—In both cases there seems to be a family predisposition.

Typhoid fever—The occurence of hyperthyroidism or of gall bladder disease following this disease is noted in every discussion of these subjects.

Cholesterol—In certain cases of nodular goitre pathologists have observed that there are large foamy cells in the acini of the thyroid. These cells contain a material which stains like lipoid material and is thought to be cholesterol ester. In lipoid gall bladder, an early manifestation of chronic inflammation, cholesterol crystals are found in the mucosa.

The basic idea of this study is to determine if these two diseases are casually related or if there is a factor common to both diseases. Sufficient material has not been considered but the investigation will be continued. It is hoped that space may permit a more complete discussion of this subject at a later date.

The writer wishes to thank Dr. Wookey and Dr. Boyd for reading the original brief and for their valuable advice and criticism.

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CORTICAL LOCALIZATION

By R. W. PRITCHARD, '41.

Cortical localization is defined as the determination of the areas of the cerebral cortex, in which are located the centres for various movements or processes.

Investigation of the cerebral cortex first came into prominence about 1870, when Hughlings Jackson pointed out the existence of a motor cortex, basing his recognition of it on a study of epilepsy in man. A study of the effects of stimulation and ablation of various parts of the cortex in man and animals, and a correlation of the varying histological structure with function, have led to a better localization of the centres.

The cerebral cortex increases in size and complexity of convolutions as we go up the phylo-genetic scale. Numerous experiments indicate also a progressive migration of the controlling centres to the cortex in higher animals, and particularly in man. Hence it will be evident that great caution is necessary in interpreting human cerebral function on the basis of animal experiments.

The histological structure of the cortex has been extensively studied by Campbell, Brodman and others, and forms the basis of the usual classification of the areas found in most physiology texts. Variations in the six typical cell layers of the cortex correlate closely with differences in function.

The Areas.

The following brief review of the areas indicates mainly the results of Foerster obtained on the human cortex.

The Frontal Lobe.

The *Motor Area* (4) lies in the front wall of the central sulcus and extends on to the free surface of the pre-central gyrus, particularly at the top, where it is continued into the paracentral lobule. This area is characterized by Betz cells which give rise to the pyramidal tracts. Galvanic stimulation produces movements of contralateral muscle groups, but bi-lateral for the face, pharynx, vocal cords and muscles of mastication. The spatial distribution of foci is in inverse order to that of the body, the cells controlling perineum, leg, trunk, arm and face being distributed in that order from above downwards. Separate foci for the fingers occupy a relatively large area in man. Single muscle twitches have been obtained here by galvanic stimulation of the dry cortex.

The *Pre-Motor Area* (6 a α) occupies the remainder of the pre-central gyrus, and is marked by the absence of Betz cells. Stimulation produces rotation of the head and eyes to the opposite side. (adversive movements) and synergic flexion and extension of the contralateral limbs through extra pyramidal tracts.

This area has been the subject of controversy lately due to Fulton's claim that lesions here produce a characteristic syndrome. However, Walshe cites a careful experiment to show that these same symptoms can be produced by lesions of the motor cortex, and it would seem from his evidence that a true "premotor syndrome" does not exist.

Area 6 a β located in the posterior part of the superior pre-frontal gyrus is excitable only with high intensity faradic current. This produces adversive movements which are still obtainable after the destruction of areas 4 and 6 a α, thus indicating that this area has its own direct pathway to the subcortical centres. Epileptiform attacks due to lesion of this area can be cured by excision without recognizable motility defects.

The *Frontal Eye field* (Area 8 a β d) is located in the posterior part of the middle pre-frontal gyrus. High galvanic or faradic current produces isolated eye movements. Excision leads to

temporary paralysis of lateral movement of the eyes to the opposite side.

Area 6 β is located in the inferior part of the pre-central gyrus. Electrical stimulation produces chewing, swallowing and licking movements. This area is unique in that continuous galvanic stimulation produces rhythmical movements which outlast the stimulus.

Epileptiform convulsions due to lesions of these areas are characterized by the movements produced by electrical stimulation. Since these convulsions usually spread to adjacent regions, it is necessary to observe the first movements of the attack in order to localize the lesion.

The *Frontal Association Areas* (9, 10, 11, 12) are located anterior to those already discussed. They are inexcitable to electrical stimulation. By a process of exclusion they have come to be regarded as the seat of intelligence. Unilateral removal in man (Jefferson, 1937) was found to be effective in curing patients with mental symptoms caused by tumours in this region. No ill effects were apparent after these operations, but it is to be noted that the subsequent occupations of these patients were not such as to reveal a failure of higher synthesis of ideas. Apparently the frontal association areas exercise an inhibitory control, for most of the above patients showed a slight freedom of manner, and in double frontal lobectomy, the patient was subsequently lacking in restraint and given to childishness. The quantity of tissue removed seems to be an important factor.

Animal experiments indicate also that unilateral lesions here produce no discoverable loss, while bilateral lesions do.

There is little evidence for left-sided dominance, this idea probably being due to observation of patients in which the lesion extended backwards into the speech area.

The Parietal Lobe.

The *Sensory Area* (1, 2, 3) is found in the post-central gyrus, and the posterior part of the para central lobule. Specific sensory foci each representing a special segment of the opposite side of the body are distributed spatially as are the motor foci of Area 4. Paraesthesia due to lesions of this area may be restricted to a very limited region (such as a band on the finger) indicating definite localization. Sensibility is partly regained after unilateral extirpation due to the existence of ipsilateral tracts.

Areas 5a and 5b are found in the remaining parts of the parietal lobe. Stimulation produces adversive movements, and also pain and paraesthesia in the opposite side (and sometimes in the bladder and rectum). Epileptic attacks originating here cause simultaneous rather than progressive paraesthesia. Area 5b may be the end of vestibular pathways since removal of a cyst here produced in the patient a sensation of turning and falling.

Head attributes a psychic function to this region, viz., that of spatial recognition and perception of relative intensity, and similarity and difference. Its central location, surrounded by the other areas, would seem to indicate that it is a correlator of the different sensory impressions.

The Temporal Lobe.

Area 22 located in the posterior part of the superior temporal gyrus has no sharply defined borders. Stimulation produces adversive movements, and the sensation of noises and obscure voices. Lesions here may produce disturbances of hearing, taste and memory. Epileptic fits originating here may be produced with experimental promptness by a sudden sharp sound. This is the *centre for hearing.*

The *centres for taste and smell* are located in the uncus and the hippocampal gyrus.

The Occipital Lobe.

The *Area Striata* (17) bordering the posterior calcarine fissure, has practically a point to point representation on the the retina, the posterior part of the area representing the more central parts of the retina. Stimulation produces the

sensation of light; destruction causes blindness.

Area 18 is located on the lateral side of the occipital lobe and contiguous with area 17. It is the *centre for interpretation of visual sensation.*

The *Occipital Eye field* (19) lies anterior to area 18. Stimulation produces movements of the eyes to the opposite side.

Stimulation of areas 18 and 19 may produce complex optical phenomena, e.g., lights, figures, stars, shiny balls, etc.

Recovery from slight lesions of the occipital area is probably only apparent, being due to readjustments which mask the defect.

Autonomic Representation in the Cerebral Cortex.

Cerebral control of the autonomic system was suspected by early investigators, but the first conclusive evidence was presented only recently (Hoff and Green, 1938). Most of the work was done on animals but the principles apply to man.

Cardiovascular Representation.

Stimulation of the *motor and pre-motor areas* (cat, monkey) with currents too weak to produce skeletal movement, caused rises of 80 to 110 mm. Hg and falls of 10 to 20 mm. Hg in blood pressure. Pressor and depressor centres were found in close proximity. Section of the vagi and splanchnic nerves abolished these responses, indicating that the effects were mediated by them.

Accelerations of 10-50% in heart rate were obtained on stimulation, accompanied by rises and falls in blood pressure.

Peripheral vascular changes were also demonstrated. Stimulation of the *pre-motor regions* produced vasoconstriction while ablation lead to vaso dilation. Peripheral vascular reflex responses to temperature changes were abolished by ablation, while a shift of the blood from the viscera to the limbs was obtained on stimulation.

Gastronomic Representation.

Cortical foci capable of controlling peristalsis have been found. Bi-lateral extirpation of the frontal lobes (monkeys) caused the animal to pass undigested food in the faeces, due to increased peristalsis. Gastric ulcer, observed in some cases of brain injury, has been attributed to gastronomic disturbance caused by autonomic unbalance.

Experiments on dogs indicate that a discrete part of the pre-motor area when stimulated causes vigorous salivation. Pupillary constriction and dilation, sweating, and erection of the hair have all been found to be disturbed by discrete lesions of the frontal lobes.

Respiratory Movements have been accelerated and inhibited by stimulation of localized regions of the cerebral cortex of the dog.

Obviously the cerebral cortex contains centres for control of the autonomic system.

Discussion.

In considering localization of function we are apt to lose sight of the cortex as a whole. While a wealth of evidence suggests that the majority of cortical fields are associated with specific function, yet the fineness of localization, and the types of function localized have to be considered.

The cortex as a whole plays an important part in facilitation, and the amount of tissue removed may be just as important as the locus of the removed area. Work on rats indicates that 20% lesion of the occipital cortex is sufficient to abolish activities analogous to reasoning, thus indicating the facilitative control of the visual cortex. Again, the severity and duration of motor aphasia after injury to the speech area varies with the extent of the destruction but is independent of the locus within the region. Partial recovery of sensation after bilateral removal of the sensory areas (1, 2, 3) is further evidence of facilitative control.

After double frontal lobectomy (man) the patient exhibited masterly (though perverted) powers of evasion when cor-

nered in an argument. Obviously the more posterior parts of the brain took over the mental activities, so that it must be supposed that these have no essential locus. We can conclude that only the motor and sensory areas are at all fixed. The brain is a vast net-work of reflexes with infinite possibilities of inhibition, adaption and substitution in mental and emotional processes, and must function intellectually and emotionally as a whole.

As to the fineness of localization; it has been pointed out that the relations between peripheral striped muscle and cortical foci are by no means as rigid as the classical theory might lead us to believe. Changes in the external conditions of the cortex (such as temperature, moisture, duration of stimulus) without compensating internal changes will cause inconstancy of the response. Thus an instability of the minuter parts exists. Foerster sums the situation nicely when he says: "We must not regard the motor cortex as a mosaic like a cubist picture, but more closely resembling the soft and merging colours of a Rafael Madonna."

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The author wishes to thank Dr. Botterell for his assistance in the preparation of the paper from which this article was condensed.

Feature Section

THE CHICAGO CONVENTION OF MEDICAL STUDENTS.

By Alfred Stein, '39.

It was my privilege, during the Christmas holidays, to attend the second annual convention of the Association of Medical Students, held in Chicago. There were registered 254 delegates, representing 37 medical schools. Being the only Canadian medical student present I felt somewhat of an outsider. However, the warm welcome I received and the spirit of enthusiasm and keen interest so manifest at the gathering soon dispelled this feeling.

The opening address by Dean Harvey of the University of Chicago Medical School sounded the keynote of the meeting. The A.M.S. was charged to keep in mind the three great objectives of organized medicine: personal, social and scientific improvement. The welcome accorded to the delegates by Dean Harvey, Dean Davis of the University of Illinois Medical School, and Dr. Olin West representing the American Medical Association together with the sponsors of the A.M.S., including Dr. Parran, Surgeon General of the United States, Dr. J. F. Fulton of Yale, Dr. Walter B. Cannon of Harvard, indicated the active interest that is being taken in the A.M.S. by eminent men in the medical profession and in the teaching world.

The co-operation of the medical profession made possible an instructive series of clinics on pediatrics, medicine, obstetrics and surgery, as well as exhibits and demonstrations. The flexible gastroscope demonstrated by the inventor, Dr. Rudolph Schindler, proved interesting. Even operating room demonstrations of the Laparotrachelotomy were planned. The invasion of movies into the field of medical education made possible two excellent motion pictures—one, the obstetrical movies of Dr. De Lee and the other on "Metrazol Treatment in the Psychoses." Never having seen a real honest-to-goodness convulsion the

latter picture was a revelation to me. The student scientific papers presented at the Conference indicated the important work medical students are contributing to scientific research.

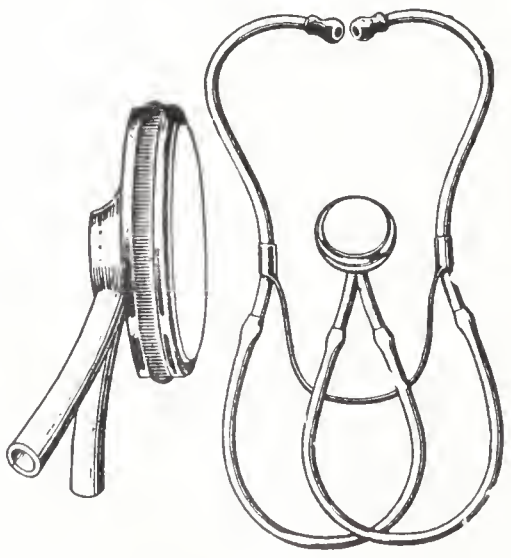
Although the Convention lasted only three days, there was in addition to the above, a tour of the American Medical Association offices in Chicago, a symposium on war, and last, but not least, a glorious New Year's Eve Ball staged in honour of "Auld Lang Syne."

But the delegates did not forget that they had assembled together to take concerted action to solve those problems that are common to medical students. The resolutions adopted by the Convention dealt for the most part with the problems of education, student welfare, interneship and co-operation between students and leaders in the profession. A permanent Student Health Committee has been set up to investigate the health conditions amongst medical students, to correlate data regarding the health of students from various Universities and to conduct a campaign for the betterment of student health. That the incidence of tuberculosis was higher among medical students than among other students, and that this deplorable situation could be remedied by proper procedures were among the findings of the committee reporting on student health. A resolution was adopted urging increased government aid to medical students in need, with the extension of government aid to medical research projects and institutions of medical education, as the necessity for such assistance may arise.

The problem of interneship was dealt with. It was decided to actively support the movement to improve the educational and health standards of internes. The convention also went on record as favouring adequate remuneration for internes.

I left Chicago feeling that I had been fortunate in attending a gathering of medical students in which there was a rich interchange of ideas between students and medical leaders from all sections of the United States and with all points of view. Indeed I felt, as Dean Harvey said in his closing address: "It will be due to the efforts of such organizations as the A.M.S. that whatever greater social happiness the future may allow will be achieved."

In the past few weeks a Canadian Association of Medical Students and Internes has been organized. I am sure that this organization will find the A.M.S. willing and eager to co-operate to the fullest extent in "endeavouring to bring about changes and reforms which concern us as deeply as they do them," (quoting from Dr. Bill King's letter in the Baltimore Convention of the A.M.S.).



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Medical Society Notes

By W. K. KERR

Already the time has come to point with pride and observe with regret the successes and short-comings of the executive for 1937-38.

The Journal, under the editorship of Bill Bigelow and his staff, continues to stand as the most notable achievement of the student body, though we are prone to take it somewhat for granted.

The event of the year was the Med-at-Home with Duke Ellington's band. The capable management of Cam Gray made this success possible.

The only time when students really feel that there is a Medical Society, is on election day and if we are to judge an election by the noise and riot attending it, then the last election was an unqualified success.

The most distinguished show on the campus, namely Daffydil, did not fail to satisfy the tastes of the stethoscopians and anybody else who could manage to get tickets for this performance. To Pete Baillie goes the credit for managing this traditional frolic with such success.

The graduation banquet this year was subsidised by the Medical Society to the extent of $100. It is hoped that this generous practice will be continued for the benefit of coming graduating classes.

In the matter of open meetings we cannot claim the success enjoyed by last year's executive.

Another phase of executive activities which has left much to be desired, is that of year dances. The only year to which we may point with pride, is 4T0. They have parties which run a close second to the "At-Home" for entertainment.

In the last month's Journal reference was made to the contemplated formation of an association of Medical Students and the general nature of such an organization was indicated. Since then definite steps have been taken along this line. The Medical Society sponsored a meeting of delegates from McGill, Queens, and Western on March 13th. At this round-table conference the skeletal structure of a national organization was formed, an executive was appointed to carry out the plans laid down and make such an organization a reality and finally the scope of the movement, its aims and more specific purposes were indicated by the delegates.

Paul McGoey, 4T0 was appointed chairman of the National Executive, Harold Copp 3T9 vice-chairman and Bill Kerr 4T0 Secretary-Treasurer.

At the time of writing the executive is waiting for the ratification of the report of the conference by other Medical Societies.

Next fall it is hoped that this Association of Canadian Medical Students and Internes will get an early and enthusiastic beginning.

In conclusion, this occasion is taken to thank Bruce Tovee, on behalf of the Medical Society for the keen interest and competent leadership which he has applied to the direction of the Medical Society Executive for 1937-38.

Medical Athletics

By W. B. CHARLES

By the time this is read university athletics will be over for another year. It has been a very active one indeed due in great measure to the re-organization of intra mural sports. Our chief interest at this time lies in the final standing of the faculties in the competition for the T. A. Reed trophy. These results are not yet complete but it would appear that Medicine will not

rank nearly as high as last year when we came third—a very worthy showing. There are several reasons for this. The chief one of course is that up to the time of writing Meds have not won a single interfaculty championship. The water polo and volley ball teams that were so successful last year have failed to repeat—the latter by the narrowest of margins and as yet no other teams have been successful. Another reason is the lack of Medical entries in the individual competitions such as the B.W. and F. assaults and the swimming meets. Some of the other faculties gain a great many points just by virtue of the great number of entries in these tournaments. It seems that interest has lagged in B.W. and F. ever since the Medical assault was abandoned. It is to be hoped that next year's executive may be able to stimulate some interest in this matter.

There are two inter-faculty championships which remain undecided, namely baseball and basketball, and for both of these Meds have an excellent chance. There are three Medical teams in basketball again this year and all three teams are in the play-offs. The Senior Meds. baseball team is also in the finals and are strongly favoured to win out. These two championships would certainly boost our standing.

We would like to say a word about this year's Medical hockey teams. Not for many years have Meds had two teams as strong, and never before have prospects looked so bright for next year. A real effort should be made to bring back the Jenning's Cup. This year's executive strongly recommends that next year the hockey teams be given the benefit of sufficient practice and efficient coaching. There is no reason why rugby should be the only team with organized coaching.

Congratulations are due to Colin "Red" Brebner. The well known rugby star is the first winner of the James Kinnear Memorial Trophy, emblematic of the squash championship of the faculty of Medicine. "Red" will have his name enscribed on the trophy and in addition will receive a handsome medal to add to his collection.

Lastly and best of all we wish through the medium of this journal to take the opportunity of congratulating on behalf not only of the Medical Athletic Association but of the whole undergraduate body, this year's recipient of the John Copp Memorial Trophy. It is a great honour for Cam and through him for the whole faculty. This is the most coveted award on the whole campus and there will never be a winner more deserving of it. It also serves, for those of us who were fortunate enough to know him, to turn our thoughts back once again to the memory of him for whom the trophy was named and we know that he would be well pleased.

Abstracts

ACUTE CHOLECYSTITIS

By James McKenty. *C.M.A.J.*. *Vol.* 38, *No.* 3, *March*, 1938, *pp.* 236.

In this stimulating article Dr. McKenty presents a plea for early operation in the treatment of acute cholecystitis. In the published reports of 3,507 cases, the vast majority of whom were operated upon after the subsidence of systemic symptoms, there were 352 deaths, a mortality of 10 per cent. That operation during the first three days of the attack might yield better results is shown by the report of 258 cases treated in this way with a mortality of only 2 per cent.

The reason for the increased mortality under the plan of delayed operation is indicated by a study of the pathological conditions disclosed by operation.

In cases operated upon during the first five days, the gall bladder lesion is found to be "uncomplicated." The gall sac is greatly distended, its wall extremely oede-

matous, and it practically always contains stones. The peritoneal coat usually retains its lustre but may present a few frail omental adhesions. The content is slightly bile-stained muco-purulent liquid. The fact that in this stage the bacterial count is often negative and always low supports the view that this is not primarily an inflammation of bacterial origin. "Acute oedema," (due to obstruction of lymph and venous channels by the stone impacted in the lower end of the gall sac), is regarded as a more appropriate name of the condition than acute cholecystitis.

Beginning about the end of the first week after the onset of colic, the condition enters the "Complicated" stage. The following complications may occur in from 15 to 30 per cent. of cases after the beginning of the second week: (a) dense adhesions to surrounding viscera; (b) gangrene of gall sac leading to rupture; (c) perforation; (d) abscess—pericholecystic, subphrenic, or hepatic; (e) peritonitis, diffuse, the most frequent cause of death; (f) pylephlebitis, a rare complication; (g) empyema of the gall bladder, present in the majority of cases operated upon during the third and fourth weeks; (h) pneumonia; (i) empyema of the right pleura.

The longer operation is delayed, the higher the incidence of complications. These complications are all highly dangerous and account for the high mortality under the delayed plan of treatment.

Dr. McKenty urges, therefore, that all cases of acute cholecystitis be operated upon during the first three to five days, with removal of the inflamed organ before the lesion has advanced to the "complicated" stage. R.A.M.

SUGGESTIONS RELATED TO THE STUDY OF SOMATIC PAIN.

By Sir Thomas Lewis, *M.D., F.R.C.P., F.R.S. British Medical Journal, Feb.* 12, 1938. *p.* 321.

The purpose of the paper is to outline certain aspects of pain from the standpoint of investigation and the extended use of the experimental method of studying pain.

Preliminary Consideration of Some Gaps in Our Knowledge.—The history of pain as detailed by an observant subject may be diagnostic of a given disturbance of a given tissue. Before the full worth of this method can be obtained description of the pain must be made more accurate. Present descriptions of pain fail to convey sufficiently precise ideas of the sensations experienced and therefore do not adequately identify them. The closer the description is to the event in time the more accurate it becomes. Another reason is the difficulty of finding right words of description and intelligent powers of observation. Descriptions of pain must comprise statements of severity, of quality, of time relation, of locality, and the circumstances in which it is felt.

Severity.—The general level of the severity of pain is recognized to be of clinical value. Standards of pain severity are, however, impossible to set up because of individual variations in experience.

Time Intensity Curve. — A diagnostic importance of a pain's duration rests in a time relation of the pain period and of its causal mechanism. The curve of pain intensity is of most importance, portraying the manner in which a pain starts, the rapidity of its culmination, the duration and smoothness at its height, and the manner of its decline.

Localization.—The value of pain localization is well known but accuracy in describing locality begins to decline from the instant it ceases. Localization should, therefore, be effected as far as possible while pain is felt. It is too generally assumed that somatic pain locates the seat of mischief since it only does this when the skin is the site of the lesion, while there is much less evidence that it does so when deeper somatic structures are concerned.

Quality.—It is my view that experience may be supplied and practice obtained in the recognition of pains of different qualities and the naming of them. Common parlance has acquired a few striking terms as "burning" or "pricking." But many terms in use such as tearing, boring, cutting, stabbing and crushing, owing to the comparative infrequency of corresponding physical damages convey as between two persons no exact ideas In illustrating and in leading up to certain suggestions and generalizations are proposed to consider pain, and especially its quality, as provoked from three somatic structures, skin, muscle and tendon or web.

Skin Pain.—Skin pain is very accurately localized, and varies in intensity and duration but not in quality. Pain can be provoked from injuring the skin in a large number of different ways, but when extraneous stimuli are excluded the irritant cannot be distinguished. A prolonged stimulus gives rise to "burning" pain and a brief one to "pricking" pain, whatever the source may be. Pain from the after effects of injury to the skin are quite indistinguishable from pain due to a present stimulus.

Muscle Pain.—This pain is more difficult to describe but is disagreeable, rather diffuse, difficult to locate, continuous, wavers a little in intensity, but has distinctive quality. Sometimes described as "aching" pain. Muscle pain is referred to a distance, i.e., from the trapezius, it is usually referred to the occiput.

Web, Tendon and Periosteal Pain.—

Pain of this quality, so called "dull" pain, is readily produced by tightly squeezing the short web of skin between two adjacent fingers. This pain has exactly the same quality no matter how it is produced. Reference sometimes occurs.

Application to Patients.—Experiments on patients chosen because they are observant, will help to solve the mechanisms of pain. Once pain is properly identified as having a "burning" quality, its origin from skin or mucous membrane is certain. Pain that is clearly recognized to have a different quality comes from deep structures and it may be recognized as derived from muscle or alternatively from one of several tissues which give rise to web pain. Pain should be named not as "stabbing" or "boring" but as skin or muscle pain. It is my view that the power to recognize pain arising from different types of tissue, can be carried to a degree of accuracy which renders it a valuable asset in investigational work. By inducing pain from skin, muscle or tendon, in an observant subject, who suffers from spontaneous pain the origin of this pain in skin, muscle or tendon may very probably be determined.

Theoretical Consideration.—In concluding that the quality of pain derived from skin or cutaneous nerve is constant and that pain of this quality is only so derived we are almost forced to infer that the relevant pain impulses are connected ultimately to special receptors in the sensorium. The difference between the quality of skin pain and of deep pain is so clear that it is possible that we are in error in classing both together under the one term "pain." Deep pain may have a separate centre in the sensorium.

J.A.G.R.

PATHOGENESIS OF HYPERTENSION.

Editorial—*J.A.M.A. Vol.* 110, *No.* 1, *Jan.* 1, 1938.

The work of Goldblatt and collaborators published in 1932 and after and showing conclusively that the kidney plays a special part in the production of high blood pressure is one of the outstanding recent contributions to medical science. A relationship between pathological changes in the kidneys and vascular disease had been suspected since the time of Richard Bright but no proof was forthcoming. Goldblatt and co-workers, using a special clamp, constricted in varying degree the main renal arteries of dogs and monkeys, thus producing the functional effect of constriction or organic narrowing of arteroles. The experimental constriction of one renal artery caused a hypertension lasting for weeks or months. On constriction of both main arteries to the kidneys the increased vascular tension induced has lasted for 5 years in some animals. By varying the degree of constriction, hypertension of benign or malignant types could be produced at will. Goldblatt at first suggested two possible mechanisms for this phenomenon: (1) Reflex nervous stimulation of the general vasomotor apparatus; (2) a humoral mechanism due to some substance either produced anew by the ischaemic kidney or accumulating in the blood as a result of failure of elimination or other cause. Results of considerable experimentation to date seem to have eliminated the possibility of a reflex nervous mechanism, leaving the humoral theory outstanding and for this, interesting experimental evidence is adduced.

Removal completely of all adrenal cortical material prevents the production of hypertension by clamping the renal arteries, but the presence of a small fragment of one adrenal cortex, barely sufficient to maintain life, permits the rise in blood pressure.

A.F.G.

THE PATHOLOGY OF GRANULOMA VENERUM.

By R. D'Annoy and E. Von Haam. *Am. Journ. of Path.. Vol.* 14. *Jan.*, 1938. *p.* 38.

Granuloma venerum, an infectious granuloma of the pudenda, is widespread in the tropics and sub-tropics. Lesions are divided into three groups: (1) those caused primarily by the infectious agent; (2) those resulting from a peculiar tissue reaction by the host; (3) those due to complications of the original infection.

In 53% of the cases studied, the serpingous type of ulcer, following the early nodular lesion, was found. The ulcer was shallow, with granulomatous, easily bleeding base, and a tendency to spread along the moist folds of the region. Healing was slow. Scars were pigmented. In 28% of the cases, there were hypertrophic tissue reactions with a mountainous "relief-map" appearance. The lesions were firm and the overlying skin usually showed the scars of previous lesions. A distinct difference was noticed between the atrophic, contracting scar which characterized the healing of the cases in the first group, and the spreading, hypertrophic scar of the cases in the second group. Secondary infection by organisms of various groups comprised about 19% of the cases.

A discussion of the causative agent was included in the report. In 8 of 11 cases, organisms of the Klebiella group were cultivated. They were demonstrable in all sections of lesions. The organisms are small, curved bacilli with capsules and polar bodies. No disease was produced on animal inoculation.

W.G.R.

TESTS FOR LIVER FUNCTION.

By A. M. Snell, M.D., and T. B. Magath. *J.A.M.A. Vol.* 110, *No.* 3, *Jan.* 15, 1938.

This excellent article is based on several thousands of tests made over a period of 5 years at the Mayo Clinic. Practically all aspects of liver function in health and disease are touched upon in the discussion of the many various liver function tests and the estimation of their clinical value. Many of these are not practical functional tests but throw some light on one or other aspect of liver disease. Bilirubin, urobilin and urobilinogen and plasma protein, cholesterol and cholesterol esters and bile salt values, laevulose and galactose tolerance, blood coagulation and haemorrhagic tendencies, phosphatase estimation, bromsulphalein elimination and hippuric acid synthesis are all discussed. The authors conclude: (1) In types of disease of the liver *not* associated with jaundice, information gained from the study of retention of bromsulphalein is as reliable as that which can be gained in any other way and that under these conditions other tests give chiefly confirmatory evidence; (2) In cases of jaundice, some information, not altogether reliable as to the possible hepatogenous or obstructive nature of the jaundice can be had from studies on the excretion of galactose, the value of cholesterol and cholesterol esters in the plasma, and the value of serum phosphatase; and (3) The best information as to the state of functional activity of the liver in cases of jaundice can be gained from a consideration of the serum bilirubin, its daily variations and a knowledge of the anatomic changes which these may represent. So far as indirect methods of measuring liver function in the presence of icterus are concerned, the hippuric acid test gives reasonably accurate results which should not, however, supplant the impressions gained from purely clinical study.

A.F.G.

MEASLES INCLUSION BODIES IN BLOOD AND TISSUE CULTURES.

By Jean Broadhurst, Gladys Cameron and Vincent Saurino. *Jour. of Infectious Diseases. Vol.* 62, *Jan.-Feb.* 1938, *p.* 7.

A summary of the research done on the infective nature of the blood of patients suffering from the disease, shows that the blood is infective for other individuals, from the appearance of symptoms to thirty hours after the appearance of the rash. A tabular summary of the evidence supporting the virus nature of the infection by showing that the blood is still infective after having passed through various filters is included.

Virus bodies (inclusion bodies and elementary bodies) are also used as evidence in supporting the aetiological role of a virus in a disease. These workers have previously shown that inclusion bodies are present in Koplik spots and the nasal mucous membranes of persons ill with measles. This report is of a further investigation to see if inclusion bodies are present in the blood during its infective stage. The investigation was done in two parts: (1) direct examination of the blood; (2) cultural methods.

On direct examination, inclusion bodies in the mononuclear cells of the blood were demonstrable in blood taken one day before the beginning of the rash to ten days after its appearance. Three types: pinpoint, globular and crescentic, were seen. Changes in the nucleoplasm and cytoplasm of the mononuclear cells were also described. Multiplication of inclusion bodies occurred in tissue culture and normal tissues inoculated with measles serum also developed similar inclusion bodies. In the tissue cultures, elementary bodies were liberated into the media.

W.G.R.

THE NUTRITIVE SIGNIFICANCE OF AMINO ACIDS.

By W. C. Rose. *Physiological Reviews.* 1938. *No.* 1.

Proteins are composed of at least twenty-two amino acids. These are produced by the digestion of food proteins, and used as substrates for the formation of many characteristic tissue proteins and many other non-protein nitrogenous components of the cells. Not all the amino-acids have the same nutritional value in the animal body. This review looks into the significance of each, and attempts to ascertain their value. Attention is directed towards their individual necessity or otherwise as dietary components.

Two methods of approach to this problem have been used by investigators. In one, some purified protein known to be deficient in one or more amino-acids is administered. In the other, hydrolysed protein from which certain known amino-acids have been eliminated, are fed. Both of these procedures have proved to be of great value.

It has been shown that some amino-acids are necessary for growth of immature animals, some necessary for life. These are grouped under the heading of *essential animo-acids.* The following ten comprise this list: lysine, tryptophane, histidine, phenylalanine, leucine, isoleucine, arginine, threonine, methionine, valine. *Arginine* is included because, although it is manufactured in the animal body, the rate of production is not sufficient to meet the demands of *normal* growth. The remaining twelve amino-acids are easily synthesised.

M.E.H.

A NEW OUTLOOK ON THE PHYSIOLOGY AND PATHOLOGY OF MENTAL AND EMOTIONAL STATES.

By Pickworth, F. A. *Brit. Med. Jour., Feb.* 5, 1938. *p.* 265.

The physiology of the relation of the complicated system of neurones, making up the central nervous system (c.n.s.), to mental function, emotional reaction, and conduct, is still obscure. Eminent scientific men have spent their lives in this research, adding greatly to our store of knowledge, but reaching only an impasse. Sherrington (1933) said: "We have to regard the relation of mind to brain as still not merely unsolved but still devoid of a basis for its very beginning." For this reason, the physiological conception of mental and emotional states (m.e.s.), forming the present basis of research might well be questioned. Might it not be that search for an infinitely complex control of the nervous system is hindering study of a humbler control by the vascular system?

Mental function is usually considered in terms of such dynamic mechanisms as nerve-muscle preparations, spinal arcs, and conditioned reflexes. However, the time relations of higher reflex action of the c.n.s., which occur practically instantaneously, are irreconciliable with those of m.e.s., which take time to develop and persist for minutes, remaining as traces perhaps for years. Thus the latter must have a different physiological basis. M.e.s. are static rather than dynamic phenomena, and are potentially independent of the higher reflexes of the c.n.s., whose metabolism they control.

None of the present theories of disordered mental states attempts to account satisfactorily for the clinical remissions and resuscitations which are universally recognized in psychiatry. Certain it is that the synaptic connections of the c.n.s. may remain intact and capable of functioning normally, although inert for many years. Lucid intervals and relapses in mentally disordered and neurological cases may well be explained by changes in the mediator of synaptic function, i.e., the m.e.s., since it is apparent that there can be no real nerve parenchymal pathology.

M.e.s. can be associated, and perhaps identified, with the capillary patterns of the cortex (mental) and brain stem (emotional), which provide an efficient and relatively simple mechanism for the actual control of the synaptic junctions of the 12,000 millions of neurones of the c.n.s. The capillary pattern, and therefore the m.e.s., existing at any time, determine the degree of inhibition or facilitation at the synapses, and hence determines conduct, the motor response characteristic of that particular m.e.s. In the brain there is selective local control of the smaller vessels by hormones, by collateral impulses from the higher reflexes of the c.n.s., and by sympathetic stimuli; metabolites and hormones sustain variations in capillary pattern so produced.

The brain capillaries are dilated by cervical sympathetic section, increased carbon dioxide, trauma, acidosis, stimulation of cranial VII, fall in blood pressure, gaseous embolism, ascetycholine, histamine, adenylic acid, nitrites, pituitrin, stimulation of the tuber cinereum or the ventral and medial thalamus, sensory stimuli, or mental effort, whereas they are constricted by decreased carbon dioxide, increased oxygen, hypertonicity of the blood, stimulation of the cervical sympathetic or the posterior hypothalamus, or adrenaline after sympathectomy or ergotamine.

Normal capillary patterns may be pathologically disrupted by head trauma, acute and chronic infections (toxins), dietary deficiencies and irregularities, digestive upsets, food poisons, undue excitement, alcoholic indulgence, worry, chronic pain stimuli, etc., with resultant alterations in m.e.s. Mental disorder may be caused by too frequent changes of m.e.s., or may result from a mixing up of normal and abnormal capillary patterns. Therefore, prophylaxis of mental disorder may well be directed to avoidance of, or skilled treatment during and after, such causes of capillary pathology. In turn, therapeusis may well be directed to the probable cause, and, in addition, include the application of drugs and treatments known to effect the capillarity of local brain areas, e.g., ergotamine, cerebral sympathectomy, etc.

"The static quality of mental and emotional states and their potential independence of the central nervous system constitute the new outlook, and are of primary importance in the correlation of the mind and its disorders with the medical sciences." F.L.L.

THE COLORIMETRIC ESTIMATION OF OESTRONE

By S. Kober; *Biochem. Journ. Feb.* 38, *p.* 357

A modification of the author's original method for the colorimetric estimation of oestrone is described, in which a 2.5% solution of naphthol in concentrated sulphuric acid is used in place of the phenol reagent. The effects of various factors on the reaction are discussed.

A method based on that of Cohen and Marrian is used for assaying urines containing little oestrone, the residual colour due to impurities being determined after destroying the characteristic oestrone colour.

Suitable methods of purification of urine extracts are described, and the error and reproducibility of the methods are discussed.

D.H.C.

STUDIES ON THE MODE OF ACTION OF SULPHANILAMIDE CULTURE ON HUMAN MARROW.

By Edwin E. Osgoode, M.D., and J. E. Brownlee. *J.A.M.A. Vol.* 110. *No.* 5, *Jan.* 29, 1938.

This article is interesting more in the methods used than in the results obtained. Living cultures of human bone marrow are inoculated with beta hemolytic streptococci in varying dosage and sulphanilamide in varying concentrations is added. Colony information, phagocytosis by leucocytes, toxicity of mixture, appearance in smear, etc., are then studied at hourly or two hourly intervals up to 24 hours or more. Among the conclusions reached in this particular article may be mentioned the following: The major action of sulphanilamide on the beta hemolytic streptococcus seemed to be neutralization of the toxins. It does not appear to kill these organisms directly although it decreases their rate of cell division, and it does permit the bactericidal properties of human serum and to some extent phagocytosis by leucocytes to kill organisms which they would be unable otherwise to destroy. It has no direct effect on phagocytosis. The effective concentration of sulphanilamide would appear to be about 1:100,000 or only one-tenth of that now ordinarily maintained in the blood stream. These conclusions may or may not be confirmed but the method of study itself seems to be a valuable one. A.F.G.

THE EFFECT OF FRUCTOSE ON THE GLUCOSE TOLERANCE CURVE

By J. P. Fletcher, and E. T. Waters, *Toronto; Biochem. Journ. Feb.* 38, *p.* 212.

Fructose, when injected intravenously into fasting rabbits, had been found by Davidson to decrease the concentration of blood glucose, and to depress the glucose tolerance curve in these animals. It was suggested that the injected fructose acted by stimulating the insulin secretion of the pancreas.

The experiments described in this paper were performed to investigate the problem further, and to test the validity of the hypothesis of Davidson. Normal dogs, and depancreatized dogs receiving a steady supply of insulin were used.

It was found that fructose, when injected intravenously, did not decrease the level of glucose in the blood, but did lower the glucose tolerance curve of normal dogs, and also of depancreatized dogs maintained on a steady supply of insulin. It was concluded from this that the effect was not due to stimulation of the pancreas to give increased secretion of insulin.

A hypothesis was advanced that fructose exercises a catalytic influence on the utilization of glucose, the site of this influence probably being in the glycogenesis mechanism of the liver. D.H.C.

THE THYROTROPIC HORMONE AND THE ANTIHORMONE PROBLEM

By S. C. Werner, New York; *Endocrin. Mar.*, 38, *p.* 291.

A sodium sulphate preparation of beef anterior pituitary, containing thyrotropic hormone, was found to produce a resistance to the thyroid stimulating effect of this extract in 10 of 11 guinea pigs treated for 39 days. This resistance or immunity to the action of the thyroptropic extract was found to develop even when small non-stimulating doses were given.

On the other hand, it was found that a flavianate extract of the same animal's pituitary, while containing active thyrotropic hormone, did not commonly produce substances in the animals which inhibited its action, and indeed caused renewed stimulation of the thyroid glands of animals which were resistant to the action of the sodium sulphate extract.

An extract was obtained which usually produced prolonged thyroid gland stimulation without the development of refractoriness or "anti-hormone." The refractoriness was thought to be an immune response to proteins associated with the hormone in the extracts. D.H.C.

EFFECT OF PRONTOSIL ON BLOOD CELLS

By Walter B. Kreutzmann and J. L. Carr. *Proc. Soc. Exptl. Biol. and Med., Feb.*, 1938.

In their experiments, the observers attempted to demonstrate cytological changes in parenchymatous organs during administration of moderate doses of prontosil and to follow the changes in the cellular elements of the blood throughout the experiments.

Twelve rabbits, of equal age, size and weight and fed on normal laboratory diet were divided into two groups of 4 and 8 animals, respectively. The former served as controls. The latter were given 0.25 gm. of prontosil per Kg. body weight for 21 days.

R.B.C., W.B.C., and platelet counts were taken daily and found to be similar in the two groups throughout the experiment. In the week following, the treated animals showed a rise of 10-15% in the red count and haemoglobin. The eosinophiles increased by about 10 to 14% and, in the second week of treatment, increased numbers of stippled erythrocytes were seen.

Microscopic examination of the tissues showed a moderate congestion of the splenic pulp with erythrocytes, and an increase in the proportion of single-lobed eosinophiles in the bone marrow.

From their results, the authors conclude that, in the dosage given, prontosil appears to act as a mild bone marrow depressant in rabbits. G.D.T.

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